## (19) World Intellectual Property Organization International Bureau



#### 

(43) International Publication Date 28 October 2004 (28.10.2004)

PCT

### (10) International Publication Number WO 2004/091548 A2

(51) International Patent Classification7:

A61K

(21) International Application Number:

PCT/US2004/009289

(22) International Filing Date: 15 April 2004 (15.04.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/462,895

15 April 2003 (15.04.2003) US

- (71) Applicant (for all designated States except US): AVALON PHARMACEUTICALS, INC [US/US]; 20358 Seneca Meadows Parkway, Germantown, MD 20876 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): STROVEL, Jeffrey, W. [US/US]; 14622 Keeneland Circlé, North Potomac, MD 20878 (US). CAIN, Colyn, B. [US/US]; 4309 Kentbury Drive, Bethesda, MD 20814 (US). HORRIGAN, Steven, K [US/US]; 1895 Millboro Drive, Potomac, MD 20854 (US). AUGUSTUS, Meena [US/US]; 3215 Hollyhock Drive, Burtonsville, MD 20866 (US).
- (74) Agents: GRANT, Alan, J. et al.; Carella, Byrne, Bain, Gilfillan, Cecchi, Stewart &, Olstein, 5 Becker Farm Road, Roseland, NJ 07068 (US).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- without international search report and to be republished upon receipt of that report
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGENETIC METHODS

(57) Abstract: Methods for identifying potential therapeutic agents, such as anti-tumor agents, based on their modulation of the expression of specified genes, especially genes mapping to specific chromosomal regions, are disclosed. Also described are methods for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes, including detecting changes in levels of gene copy number and/or level of amplification of the said gene, or sets of genes, to detect and/or diagnose the cancer. Methods for detecting or determining functionally related genes, as well as methods for treating cancer based on targeting expression products of such genes, determining genes involved in the cancerous process and the success and/or response rates and survival statistics for cancer patients on treatment are encompassed by the invention. Also encompassed are methods involving determining the modulated expression of the genes in these regions of interest (ROIs) as pharmacodynamic/pharmacogenetic/surrogate markers and/or for patient profiling prior to accrual for clinical trials/treatments based on the identification of these genes as validated gene/drug targets in various cancer tissue types.

) 2004/091548

THIS PAGE BLANK (USPTO)

WO 2004/091548

PCT/US2004/009289

# DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGENETIC METHODS

5

This application claims priority of U.S. Provisional Application Serial No. 60/462,895, filed 15 April 2003, the disclosure of which is hereby incorporated by reference in its entirety.

15

20

25

#### FIELD OF THE INVENTION

The present invention relates to identification of genes whose disruption and/or change in expression is useful to distinguish cancerous from non-cancerous tissue and serve as potential therapeutic targets, pharmacodynamic /pharmacogenetic/surrogate and prognostic and diagnostic markers, and which genes are identified by high resolution Comparative Genomic Hybridization (CGH) and Spectral Karyotyping (SKY)/fluorescent *in situ* hybridization (FISH) analysis of DNA and chromosomes of various cancer cell lines and primary and metastatic tumor samples combined with gene expression analysis of these cells and tissues.

30

35

#### **BACKGROUND OF THE INVENTION**

Chromosomal abnormalities have been identified in most cancer cells. Conventional chromosome banding techniques allow for the detection of specific chromosomal defects in tumor cells but interpretation of the banding pattern is sometimes difficult, particularly when complex chromosomal

5

10

15

30

rearrangements or subtle abnormalities are present. In recent years, new techniques, such as CGH and SKY, based on fluorescent *in situ* hybridization (FISH) (Pinkel et al., Proc Nat Acad Sci USA 85:9138-42 (1988)) have been developed to overcome the limitations of conventional chromosome banding. CGH measures intensities of fluorescently labeled tumor DNA and normal DNA following hybridization to normal chromosomes (Kallioniemi et al., Science 258:818-21 (1992)). Gain or loss of copy number of a particular chromosome or chromosome region in the tumor DNA is determined by the relative intensity of a fluorescence ratio. SKY utilizes a cocktail of chromosome probes, fluorescently labeled to specify each chromosome, which is hybridized to tumor chromosomes in an effort to identify numerical and structural abnormalities in the tumor cell (Schröck et al., Science 273:494-7 (1996)). CGH and SKY have been used to identify chromosomal regions that harbor genes significant to the process of tumor initiation or progression.

#### **BRIEF SUMMARY OF THE INVENTION**

In one aspect the present invention relates to a set of genes that have been localized within human chromosomal regions of interest (ROI) that have been identified by molecular cytogenetic techniques.

In one aspect, the present invention relates to a method for diagnosing cancer in a mammal, especially a human patient, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

In a preferred embodiment thereof, the cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

In another preferred embodiment thereof, 3. The method of claim 1 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 – 805 and 855 - 923.

5

10

15

20

:25

30

In another embodiment, the present invention relates to a method for diagnosing cancer or a pre-cancerous condition in a mammal, comprising:

- (a) obtaining a cell or tissue sample from a mammal, especially a human patient, suspected of having cancer or a pre-cancerous condition and determining for said sample the gene copy number of a gene of Table 1;
- (b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

and the state of the second of the property between the second second second second second second second second

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

In a preferred embodiment of the methods of the invention, said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

In another embodiment, the present invention relates to a method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

- (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;
  - (b) administering said test compound to said patient;
- (c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

5

20

30

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

In a further embodiment, the present invention relates to a method for identifying an antineoplastic agent, comprising:

- (a) contacting a test compound with a cell that expresses a gene of Table 1; and
- (b) determining a change in gene expression as a result of said10 contacting;

whereby said change in said gene expression identifies said test compound as an antineoplastic agent.

The present invention also relates to a method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous.

In an additional embodiment, the present invention relates to a method for identifying a compound as an anti-neoplastic agent, comprising:

- (a) contacting a test compound with a polypeptide encoded by a gene of Table 1,
- (b) determining a change in a biological activity of said polypeptide due to said contacting,

wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

In a preferred embodiment of the foregoing, the polypeptide is an enzyme selected from kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase. transferase, deacetylase and polymerase.

The present invention also relates to a method for identifying an antineoplastic agent comprising contacting a cancerous cell with a compound found to have anti-neoplastic activity in other the methods of the invention under conditions promoting the growth of said cell and detecting a change in the activity of said cancerous cell.

The present invention further relates to a method for treating cancer comprising contacting a cancerous cell with an agent having affinity for an expression product of a gene of Table 1 and in an amount effective to cause a reduction in cancerous activity of said cell.

The present invention also contemplates a method for monitoring the progress of cancer therapy in a patient comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1.

15

20

25

30

10

5

In addition, the present invention encompasses a method for determining the likelihood of success of cancer therapy in a patient, comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1 wherein a decrease in said expression prior to completion of said cancer therapy is indicative of a likelihood of success of said cancer therapy.

In another embodiment, the present invention relates to a method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

- (a) identifying a test compound as having anti-neoplastic activity using other methods of the invention;
- (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.

Additionally, the present invention encompasses a method for determining the progress of a treatment for cancer in a patient afflicted therewith, following commencement of a cancer treatment on said patient, comprising:

- (a) determining in said patient a change in expression of one or more genes of Table 1; and
- (b) determining a change in expression of said gene compared to expression of said one or more determined genes prior to said cancer treatment;

wherein said change in expression indicates progress of said treatment thereby determining the progress of said treatment.

#### SEQUENCE LISTING ON CD-ROM ONLY

15

20

30

10

5

The sequences disclosed herein as SEQ ID NO: 1-923 in the sequence listing are contained on compact disc (CD-ROM) only, which accompanies this application and the contents of said CD-ROMs are hereby incorporated by reference in their entirety. These sequence numbers also appear in Table 1 where all sequences are referred to as consecutive serial numbers for reference purposes only.

#### 25 **DETAILED SUMMARY OF THE INVENTION**

The present invention relates to a set of genes that are amplified and/or over-expressed genes in cancer cell lines and have been localized to various chromosomal regions of interest. These genes have been identified through a combination of CGH, SKY, expression analysis and Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Such genes are both markers and potential therapeutic targets for cancer, in particular breast,

colon, lung and prostate malignancies. In addition, the amplified nature of such genes provides a means of diagnosing a cancerous condition, or predisposition to a cancerous conditions, by determining the amplification of one or more of such genes in a patient afflicted with, or predisposed toward, or otherwise at risk of developing, cancer.

In accordance with the present invention, a number of genes have been localized to a chromosomal regions of interest as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate), serial number 806-923 (transcript or protein)). The invention also includes any subsets of these. As described herein, these sequences include DNA sequences of SEQ ID NO: 1 – 805, transcripts with the sequences of SEQ ID NO: 855 – 923, and proteins/polypeptides with amino acid sequences of SEQ ID NO: 806 - 854.

15

20

25

10

5

Briefly, the procedures used to identify the genes disclosed herein may be summarized as follows:

For CGH analysis, based on detailed molecular cytogenetic characterizations, the following data sets are generated, which may include regions reported in the public domain as well as unique regions not previously known.

- 1. A map of chromosomal regions involved in consistent, recurrent and high level genomic gains (i.e., amplifications) for a representative cancer cell line or tumor type (e.g. colon, prostate, breast and lung) that can be recognized as a pattern/signature for a given tumor type.
- 2. A map of chromosomal regions containing genomic losses (i.e., deletions) in each tumor type and individual cell line to be examined.
- 3. Levels of intensities of gains and losses categorized for entry into a database.

5

10

20

25

30

4. A comparison of the patterns of gains and losses between the clinical samples (e.g. colon xenografts) and cell lines (e.g., colon) of matched Stages and Grades.

5. A comparison of the patterns of gains and losses between primary prostate tumor cell lines (e.g., CPDR lines) and metastatic prostate tumor cell lines (e.g., DU 145, PC3 and LNCaP).

In accordance with the present invention, for SKY analysis, data sets were generated according to the following steps:

- 1. Identification and development of a database of novel chromosomal rearrangements in epithelial cancer cell lines.
  - 2. Identification of novel translocations involving specific chromosomes or chromosomal regions
- Reconciliation of SKY and CGH analysis on the same cell line as a
   verification of the combined findings.

Combining genomic DNA analysis of gains and losses in the tumor cell lines/clinical samples with cDNA expression analysis from matched tumor types displayed on a genome template from the Golden Path genome browser using a Spotfire<sup>TM</sup> analysis tool:

- A pattern of gene expression on a U-95 Affymatix chip set obtained via the Gene Logic database was used to generate differential gene expression profiles between samples sets containing normal and malignant tissues from colon, prostate, lung, breast and various cell lines.
- 2. A Spotfire™ visualization tool was developed that allowed the generation of a list of all the genes that are present in the Golden Path within the clustered regions of gains/losses for each cell type/tumor type to generate the gene sets to include in the HITS platform
- 3. The following algorithm was employed:

5

.10

15

20

. . 25

.30

i) Match chromosomal regions of amplification/gains defined by CGH with the location of genes/ESTs on an Affymatix chip as mapped to a Golden Path genome template.

- ii) Identify genes/ESTs over-expressed in tumor tissue compared to normal tissue in said chromosomal regions using the Gene Logic database.
- iii) Compile data on cell lines of a particular tumor type and different tumor types showing clusters of genomic gains and losses at certain chromosomal regions.
- iv) Pick BACs that span the chromosomal regions consistently gained and containing over-expressed genes in an effort to positionally clone novel cancer genes (oncogenes and genes in relevant pathways)
  - Validate the identified genes by
     A) Picking STS markers that identify the gene sequence and quantify the relative copy number in genomic DNA and RNA across a panel of tumor cell lines.
    - B) Develop probes for FISH on chromosomes from tumor cell lines and primary tumor tissue micro-arrays.
- 4. The expression data from tumor cell lines that have undergone SKY/CGH analysis was used to pick candidate genes to validate as individual targets in functional genomic assays and in-vivo assays and for use in the transcriptional assay platform.

In accordance with the present invention, over-expression of cellular genes is conveniently monitored in model cellular systems using cell lines (such as is used in the example below), primary cells, or tissue samples maintained in growth media. For different purposes, these may be treated with compounds at one or more different concentrations to assay for modulating agents. Thus, cellular RNAs were isolated from the cells or cultures as an indicator of selected gene expression. The cellular RNAs were then divided

and subjected to analysis that detected the presence and/or quantity of specific RNA transcripts, which transcripts were then amplified for detection purposes using standard methodologies, such as reverse transcriptase polymerase chain reaction (RT-PCR). The levels of specific RNA transcripts, including their presence or absence, were determined. When used for identification of modulating agents, such as anti-neoplastic agents, a metric is derived for the type and degree of response of the treated sample compared to control samples.

In accordance with the foregoing, the genes identified as being amplified and/or over-expressed, which can include increased copy number thereof, in cancerous cells are localized in chromosomal regions of interest as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); for polypeptide SEQ ID NOs, see Table 1, serial number 806-923 (transcript or protein)).

These genes may be utilized to characterize, the cancerous, or non-cancerous, status of cells, or tissues. The methods of the invention may be used with a variety of cell lines or with primary samples from tumors maintained *in vitro* under suitable culture conditions for varying periods of time, or *in situ* in suitable animal models.

The genes disclosed herein are expressed at levels in cancer cells that are different from the expression levels in non-cancer cells. These genes as identified in Table 1 are amplified in cancer cells relative to non-cancer cells of corresponding tissues, especially breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

20

25

5

In accordance with the foregoing, the present invention relates to a method for diagnosing cancer in a mammal, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

5

In a preferred embodiment thereof, said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 – 805 and 855 - 923. In a further preferred embodiment, said mammal is a human patient.

10

15

20

The present invention is also directed to a method for diagnosing cancer or a pre-cancerous condition in a mammal, preferably a human patient, comprising:

- (a) obtaining a cell or tissue sample from a mammal suspected of having cancer or a pre-cancerous condition and determining for said sample the gene copy number of a gene of Table 1;
  - (b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

25

In specific embodiments, the cancer to be diagnosed is one or more of breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

Preferably, the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 – 805 and 855– 923.

5

10

15

25

The present invention is also directed to a method of inhibiting cancer, or a pre-cancerous condition, in a mammalian cell, comprising contacting said cell with a molecule that inhibits function of a gene of Table 1. Preferably, the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923. In a specific embodiment thereof, said molecule inhibits gene function by binding to said gene. In other embodiments, the molecule inhibits gene function by binding to an RNA encoded by said gene or inhibits gene function by binding to polypeptide encoded by said gene. Preferably, the molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA. Also preferred is where the cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

The invention contemplates that such contacting occurs in vivo.

The invention also relates to a method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

- 20 (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;
  - (b) administering said test compound to said patient;
  - (c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

Preferably, said therapeutic activity is anticancer activity and said cancer is one or more of breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

5

10

20

25

30

Also preferred is where said gene product is an RNA or a polypeptide, especially where an activity of the polypeptide is determined, preferably an enzyme activity. In specific embodiments, said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 – 923, as well as where said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

The present invention also relates to a method for identifying an antineoplastic agent, comprising:

- (a) contacting a test compound with a cell that expresses a gene of Table 1; and
- (b) determining a change in gene expression as a result of said contacting;

whereby said change in said gene expression identifies said test compound as an antineoplastic agent.

Most preferred is where the change in expression is a decrease in expression. The contacting may occur *in vivo*. Also preferred is where said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 – 923 and where said molecule is a member selected from an antisense DNA, an antisense RNA, ribozyme, an siRNA, a small organic molecule and an antibody.

The present invention also relates to a method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous. Preferably, wherein said elevated expression is an elevated copy number of the gene and wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

The present invention further relates to a method for identifying a compound as an anti-neoplastic agent, comprising:

- (a) contacting a test compound with a polypeptide encoded by a gene of Table 1,
- 5 (b) determining a change in a biological activity of said polypeptide due to said contacting,

wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

10 Preferably, said gene of Table encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

In a preferred embodiment, the change in biological activity is a decrease in biological activity.

15

In another preferred embodiment, the biological activity is an enzyme activity, such as where the enzyme is one selected from the group kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase, transferase, deacetylase and polymerase.

20

25

30

Assays for these enzymes available. are such as for phosphodiesterases (the most pharmacologically relevant phosphodiesterases are those that hydrolyze cyclic nucleotides (see, for example, cAMP and cGMP assays available from Perkin-Elmer, as well as Estrade et al., Eur. J. Pharmacol. 352:2-3, 157-163 (1998)).

Protein phosphatases remove phosphate residues from proteins. Most tests of their activity use the same assays as for protein kinases. A non-radioactive phosphatase assay system is available from Promega Biotech.

5

10

15

20

25

30

The therapeutically most relevant dehydrogenases oxidize or reduce small molecular weight metabolites, esp. steroid hormones, or that generally use or generate NAD or NADP (see: Haeseleer et al., J. Biol. Chem., 273:21790-21799 (1998)). A commercial assay is available from Cayman Chemical (at www.caymanchem.com).

Gamma-carboxylases are important enzymes in the blood coagulation process. The main assay protocols use synthetic peptides (see: Ulrich et al., J. Biol. Chem., 263:9697-9702 (1988); Begley et al., J. Biol. Chem., 275:36245-36249 (2000)).

Sand Sand Commence of the Commence of the Sand Sand Sand Sand Sand Sand Sand

In highly preferred embodiments, the kinase is one of a protein kinase, a serine or threonine kinase, or a receptor tyrosine protein kinase. Where the polypeptide encoded by a gene of the invention is a protein kinase, especially involving tyrosine kinase, various assays for activity are available. Protein kinases add phosphate groups to serine, threonine or tyrosine residues on proteins, most commonly measured with phospho-serine, threonine, or tyrosine-specific antibodies, or generation of radiolabeled substrate, or consumption of ATP, or phosphorylation of (synthetic) small peptides, or measuring downstream enzyme activity and gene transcription. Such assays are commercially available. (See, for example, the tyrosine kinase assay from Roche Molecular Biochemicals). Assays for serine/threonine kinases are also available at Chromagen.com, Upstate Biotechnology, Inc. (Lake Placid, NY, and at upstatebiotech.com) and from Applied BioSystems (Foster City, CA (home.appliedbiosystems.com)).

In other specific embodiments, the protease is a serine protease, cysteine protease or aspartic acid protease, or the transferase is a methyltransferase, preferably a cytosine methyltransferase or an adenine methyltransferase, or the deacetylase is a histone deacetylase, or the

carboxylase is a  $\gamma$ -carboxylase, or the peptidase is a zinc peptidase, or the polymerase is a DNA polymerase or an RNA polymerase.

Proteases degrade proteins, un-specifically or at specific sites. Almost all pharmacologically relevant ones have very narrowly defined specific substrates, and their activity is most often measured by directly measuring cleavage product or generation of (fluorescent) light after cleavage of synthetic substrates. Assays are available for serine proteases (Calbiochem, Palo Alto, CA, and see Berdichevsky et al., J. Virol. Methods, 107:245-255 (2003), for systeine proteases (See: Schulz et al., Mol. Pathol., 51:222-24 (1998) and Selzer et al., PNAS, 96:11015-11022 (1999)), for aspartic acid proteases (Geno Tech, Inc. at www.genotech.com) and for zinc peptidases (see Evans et al., J. Biol. Chem., 278:23180-23186 (2003)).

15

10

5

Both (regulatory) DNA-methylases and (biosynthetic) protein methylases that are drug targets. (See: Jonassen and Clarke, J. Biol. Chem., 275:12381-12387 (2000); Jackson et al., Nature, 416:556-560 (2002)).

20

25

30

Most HDAC (histone deacetylase) assays use colorimetric or fluorometric (synthetic) substrates. Standard assays are for binding, especially molecular size changes, blocking a specific site, and effects on transcription or downstream reactions (if DNA or RNA is the direct target of a drug). A commercial assay is available from Vinci Biochem (at www.vincibiochem.it).

į

In another specific embodiment, the biological activity is a membrane transport activity, preferably wherein the polypeptide is a cation channel protein, an anion channel protein, a gated-ion channel protein or an ABC

transporter protein. Drug effects on the activity of transporter and channel proteins are screened by measuring increase or decrease of the ((radio-)labeled) transported entity inside or outside the cell, in cell-based assays, ATP consumption (in the case of ATPases), or changes in cell membrane potential. Assays employing such proteins are available, such as for ABC transporter (see: Marcil et al., Lancet, 354:1341-46 (1999) and for ion channels (from Evotec OAI, at www.evotecoai.com and from PharmaLinks, at www.pharmalinks.org/research/cellsignalling).

5

10

15

20

25

In one embodiment, the polypeptide is an integrin (the signal transduction pathways elicited by the integrins are slow and not very well characterized, hence most assays are either just binding assays or measure downstream biological phenomena (such as migration, invasion, etc.) (See: Ganta et al., Endocrinology, 138:3606-3612 (1997); Sim et al., J. Biomed. Mater. Research, 68A:352-359 (2004); and Weinreb et al., Anal. Biochem., 306:305-313 (2002)), or a Cytochrome P450 enzyme (almost all cytochrome assays require knowledge of what the substrate is and measure conversion of substrate (free or (radio-)labeled) or generation of product; useful C<sup>14</sup>-labeled substrates are available from Amersham Biosciences at www1.amershambiosciences.com), or a nuclear hormone receptor (Assays available from Discoverx, Fremont, CA, such as an estrogen assay; also see Rosen et al., Curr. Opin. Drug. Discov. Devel., 6:224-30 (2003)).

In one preferred embodiment, the biological activity is a receptor activity, preferably where the receptor is a G-protein-coupled receptor (GPCR).

GPCRs are transmembrane proteins that wind 7 times back and 30 forth through a cell's plasma membrane with a ligand binding site located on the outside of the membrane surface of the cell and the effector site

being present inside the cell. These receptors bind GDP and GTP. In response to ligand binding, GPCRs activate signal transduction pathways which induce a number of assayable physiological changes, e.g., an increase in intracellular calcium levels, cyclic-AMP, inositol phosphate turnover, and downstream gene transcription (directly or via reporterassays) along with other translocation assays available for measuring GPCR activation when the polypeptide encoded by a gene of the invention is a GPCR. Thus, such proteins work through a second messenger. The result is activation of CREB, a transcription factor that stimulates the production of gene products. One useful assay is the so-called BRET2/arrestin assay, useful in screening for compounds that interact with GPCRs. (See: Bertrand et al, J. Recept. Signal Transduct Res., 22:533-41 (Feb.-Nov. 2002)). In addition, numerous assays are commercially available, such as the Transfluor Assay, available from Norak Biosciences, Inc. (www.norakbio.com) or ArrayScan KineticScan, both from Cellomics, or assays from CyBio (Jena, Germany).

Assays useful with the invention are usually set up to screen for agonists or antagonists after adding ligand, but effects on most of these parameters can be measured whether or not the ligand for the receptor is known. Such assays may involve radioligand-binding assays. Activation of the majority of GPCRs by agonists leads to the interaction of beta-arrestin (a protein that is involved in receptor desensitization and sequestration) with the receptor, which is measurable by fluorescence energy transfer

25

30

20

5

10

15

The disclosure of all journal articles, or other publications, referred to herein are hereby incorporated by reference in their entirety.

In one embodiment, the polypeptide is in a solution or suspension and contact with the test compound is by direct contact between the test compound and the protein molecule. Alternatively, the polypeptide may be in

a cell and the test compound may have to diffuse into the cell in order to contact the polypeptide. In an alternative embodiment, the test compound may be contacted with a cell that contains or expresses the polypeptide but the test compound may have no direct contact with the polypeptide. In stead, the test compound may act to induce production and/or activity of a different compound, such as an intracellular second messenger that serves to contact the polypeptide and modulate or change the biological activity of this polypeptide.

5

10

15

20

25

30

In accordance with the foregoing, the method of the present invention includes cancer modulating agents that are themselves either polypeptides, or small chemical entities, that affect the cancerous process, including initiation, suppression or facilitation of tumor growth, either *in vivo* or *ex vivo*. Such agents may also be antibodies that react with one or more polypeptides encoded by genes as disclosed herein, preferably polypeptides comprising any one of the amino acid sequences of SEQ ID NO: 806 – 854.

the second profite exercises on the contract of the second of the second

Because the genes disclosed herein are over-expressed and relate to the cancerous condition of a cell, successful anti-neoplastic activity will commonly be exhibited by agents that reduce the expression of said genes as identified in Table 1. In one embodiment thereof, the change in expression is a decrease in copy number of the gene or genes under study. In accordance therewith, said change in gene copy number is conveniently determined by detecting a change in expression of messenger RNA encoded by said gene sequence. In another preferred embodiment, expression is determined for more than one such gene, such as 2, 5, 10 or more of the genes.

Other methods useful in measuring a change in expression of the genes disclosed herein include measuring a change in the amount or rate of synthesis of a polypeptide encoded by said gene, preferably a decrease in synthesis of said polypeptide. Most preferably, the polypeptide comprises an

5

10

15

20

25

30

amino acid sequence highly homologous to a sequence for genes as identified in Table 1 (SEQ ID NO: 1-923).

The methods of the invention can thus be utilized to identify antineoplastic agents useful in treatment of cancerous conditions. Such activity can be further modified by first identifying such an agent using an assay as already described and further contacting such agent with a cancerous cell, followed by monitoring of the status of said cell, or cells. A change in status indicative of successful anti-neoplastic activity may include a decrease in the rate of replication of the cancerous cell(s), a decrease in the total number of progeny cells that can be produced by said cancerous cell(s), or a decrease in the number of times said cancerous cell(s) can replicate, or the death of said cancerous cell(s).

Anti-neoplastic agents may also be identified using recombinant cells suitably engineered to contain and express the cancer-related genes disclosed herein. In one such embodiment, a recombinant cell is formed using standard technology and then utilized in the assays disclosed herein. Methods of forming such recombinant cells are well known in the literature. See, for example, Sambrook, et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, N.Y., (1989), Wu et al, *Methods in Gene Biotechnology* (CRC Press, New York, NY, 1997), and *Recombinant Gene Expression Protocols*, in *Methods in Molecular Biology*, Vol. 62, (Tuan, ed., Humana Press, Totowa, NJ, 1997), the disclosures of which are hereby incorporated by reference.

The present invention also relates to a method for detecting the cancerous status of a cell, comprising detecting elevated copy number and/or expression in said cell of at least one gene that maps to the chromosomal region of interest as identified in Table 1 (SEQ ID NO: 1-923). Such elevated expression may be readily monitored by comparison to that of otherwise normal cells having the same genes. Elevated expression of these

genes is indicative of the cancerous state. This includes a gene corresponding to a polynucleotide that comprises a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1-923). Such elevated expression, including increased copy number, may be the expression of more than one such gene.

The present invention also relates to a method for detecting a cancer-linked gene comprising the steps of contacting a compound identified as having gene modulating activity for a gene corresponding to a polynucleotide that comprises a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 – 923) with a cell expressing a test gene and detecting modulation, such as decreased activity, of such test gene relative to when said compound is not present thereby identifying said test gene as a cancer-related gene. In preferred embodiments, the gene determined by said method is an oncogene, or cancer facilitating gene.

In another embodiment, there is provided a method for treating cancer comprising contacting a cancerous cell with an agent first identified as having gene modulating activity using any of the assay methods disclosed according to the invention and in an amount effective to reduce the cancerous activity of said cell. In a preferred embodiment, the cancerous cell is contacted *in vivo*. In other preferred embodiments, said reduction in cancerous activity is a decrease in the rate of proliferation of said cancerous cell, or said reduction in cancerous activity is the death of said cancerous cell.

25

30

20

5

10

The present invention further relates to a method for treating cancer comprising contacting a cancerous cell with an agent having activity against an expression product encoded by a gene corresponding to a polynucleotide comprising a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 – 923)where the product is a polypeptide, most preferably one comprising an amino acid sequence as identified in Table 1 (SEQ ID NO: 806 - 854). In a

preferred embodiment, said cancerous cell is contacted *in vivo*. In another preferred embodiment, the agent is an antibody.

As noted, the genes useful in the assay methods include genes mapping within chromosomal regions of interest and genes as identified in Table 1 (SEQ ID NO: 1-923), or a gene that encodes the same RNA, such as the same messenger RNA, whose corresponding cDNA is one of the sequences as identified in Table 1 (SEQ ID NO: 1-923). The genes useful in the methods of the invention further include genes encoding RNAs whose corresponding cDNA is at least 90% identical to a sequence as identified in Table 1 (SEQ ID NO: 1-923), preferably at least about 95% identical to such a sequence, more preferably at least about 98% identical to such sequence and most preferably one comprising that sequence are specifically contemplated by all of the methods of the present invention.

15

10

5

In addition, sequences encoding the same proteins (SEQ ID NO: 806 – 854) as any of these sequences, regardless of the percent identity of such sequences, are also specifically contemplated by the invention.

The sequences disclosed herein may be genomic in nature and thus 20 represent the sequence of an actual gene, such as a human gene, or may be a cDNA sequence derived from a messenger RNA (mRNA) and thus represent contiguous exonic sequences derived from a corresponding genomic sequence or they may be wholly synthetic in origin for purposes of testing. As described in the Example, the expression of these cancer-related **25** . genes is determined from the relative expression levels of the RNA complement of a cancerous cell relative to a normal (i.e., non-cancerous) cell. Because of the processing that may take place in transforming the initial RNA transcript into the final mRNA, the sequences disclosed herein may represent less than the full genomic sequence. They may also represent sequences 30 derived from ribosomal and transfer RNAs. Consequently, the genes present in the cell (and representing the genomic sequences) and the sequences

disclosed herein, which are mostly cDNA sequences, may be identical or may be such that the cDNAs contain less than the full genomic sequence. Such genes and cDNA sequences are still considered corresponding sequences because they both encode similar RNA sequences. Thus, by way of nonlimiting example only, a gene that encodes an RNA transcript, which is then processed into a shorter mRNA, is deemed to encode both such RNAs and therefore encodes an RNA complementary to (using the usual Watson-Crick complementarity rules), or that would otherwise be encoded by, a cDNA (for example, a sequence as disclosed herein). Thus, the sequences disclosed herein correspond to genes contained in the cancerous or normal cells used to determine relative levels of expression because they represent the same sequences or are complementary to RNAs encoded by these genes. Such genes also include different alleles and splice variants that may occur in the cells used in the methods of the invention.

15

20

25

30

10

5

The genes of the invention "correspond to" a polynucleotide having a sequence as identified in Table 1 (SEQ ID NO: 1-923) if the gene encodes an RNA (processed or unprocessed, including naturally occurring splice variants and alleles) that is at least 90% identical, preferably at least 95% identical, most preferably at least 98% identical to, and especially identical to, an RNA that would be encoded by, or be complementary to, such as by hybridization with, a polynucleotide having the indicated sequence. In addition, genes including sequences at least 90% identical to a sequence as identified in Table 1 (SEQ ID NO: 1 - 923), preferably at least about 95% identical to such a sequence, more preferably at least about 98% identical to such sequence and most preferably comprising such sequence are specifically contemplated by all of the methods of the present invention as being genes that correspond to these sequences. In addition, sequences encoding the same proteins as any of these sequences, regardless of the percent identity of such sequences, are also specifically contemplated by any of the methods of the present invention that rely on any or all of said sequences, regardless of how they are otherwise described or limited. Thus,

any such sequences are available for use in carrying out any of the methods disclosed according to the invention. Such sequences also include any open reading frames, as defined herein, present within any of the sequences as identified in Table 1 (SEQ ID NO: 1 – 805 and 855 - 923).

5

10

30

Further in accordance with the present invention, the term "percent identity" or "percent identical," when referring to a sequence, means that a sequence is compared to a claimed or described sequence after alignment of the sequence to be compared (the "Compared Sequence") with the described or claimed sequence (the "Reference Sequence"). The Percent Identity is then determined according to the following formula:

#### Percent Identity = 100 [1-(C/R)]

wherein C is the number of differences between the Reference Sequence and the Compared Sequence over the length of alignment between the Reference Sequence and the Compared Sequence wherein (i) each base or amino acid in the Reference Sequence that does not have a corresponding aligned base or amino acid in the Compared Sequence and (ii) each gap in the Reference Sequence and (iii) each aligned base or amino acid in the Reference Sequence that is different from an aligned base or amino acid in the Compared Sequence, constitutes a difference; and R is the number of bases or amino acids in the Reference Sequence over the length of the alignment with the Compared Sequence with any gap created in the Reference Sequence also being counted as a base or amino acid.

If an alignment exists between the Compared Sequence and the Reference Sequence for which the percent identity as calculated above is about equal to or greater than a specified minimum Percent Identity then the Compared Sequence has the specified minimum percent identity to the Reference Sequence even though alignments may exist in which the

hereinabove calculated Percent Identity is less than the specified Percent Identity.

As used herein, the terms "portion," "segment," and "fragment," when used in relation to polypeptides, refer to a continuous sequence of residues, such as amino acid residues, which sequence forms a subset of a larger sequence. For example, if a polypeptide were subjected to treatment with any of the common endopeptidases, such as trypsin or chymotrypsin, the oligopeptides resulting from such treatment would represent portions, segments or fragments of the starting polypeptide. When used in relation to a polynucleotide, such terms refer to the products produced by treatment of said polynucleotides with any of the common endonucleases, or any stretch of polynucleotides that could be synthetically synthesized.

As used herein, the term "DNA segment" or "DNA sequence" refers to a DNA polymer, in the form of a separate fragment or as a component of a larger DNA construct, which has been derived from DNA, and may include both single stranded and duplex sequences. Such segments are provided in the form of an open reading frame uninterrupted by internal non-translated sequences, or introns, which are typically present in eukaryotic genes.

20

15

5

10

The term "coding region" refers to that portion of a gene which either naturally or normally codes for the expression product of that gene in its natural genomic environment, i.e., the region coding *in vivo* for the native expression product of the gene.

.25

30

The term "nucleotide sequence" refers to a heteropolymer of deoxyribonucleotides. Generally, DNA segments encoding the proteins provided by this invention are assembled from cDNA fragments and short oligonucleotide linkers, or from a series of oligonucleotides, to provide a synthetic gene which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon.

The term "expression product" means that polypeptide or protein that is the natural translation product of the gene and any nucleic acid sequence coding equivalents resulting from genetic code degeneracy and thus coding for the same amino acid(s).

The term "fragment," when referring to a coding sequence, means a portion of DNA comprising less than the complete coding region whose expression product retains essentially the same biological function or activity as the expression product of the complete coding region.

The present invention also finds use as a means of diagnosing the presence of cancer in a patient, as where a sample of cancerous tissues or cells, or tissues or cells suspected of being cancerous. For such purposes, and in accordance with the disclosure elsewhere herein, such diagnosis is based on the detection of elevated expression or amplification, such as elevated copy number, of one or more of the genes identified according to the invention. Such elevated expression can be determined by any of the means described herein.

20

25

30

5

10

15

In one such embodiment, the elevated expression, as compared to normal cells and/or tissues of the same organ, is determined by measuring the relative rates of transcription of RNA, such as by production of corresponding cDNAs and then analyzing the resulting DNA using probes developed from the gene sequences as identified in Table 1. Thus, the levels of cDNA produced by use of reverse transcriptase with the full RNA complement of a cell suspected of being cancerous produces a corresponding amount of cDNA that can then be amplified using polymerase chain reaction, or some other means, such as rolling circle amplification, to determine the relative levels of resulting cDNA and, thereby, the relative levels of gene expression.

For RNA analysis, the latter may be isolated from samples in a variety of ways, including lysis and denaturation with a phenolic solution containing a chaotropic agent (e.g., triazol) followed by isopropanol precipitation, ethanol wash, and resuspension in aqueous solution; or lysis and denaturation followed by isolation on solid support, such as a Qiagen resin and reconstitution in aqueous solution; or lysis and denaturation in non-phenolic, aqueous solutions followed by enzymatic conversion of RNA to DNA template copies. Steady state RNA levels for a given type of cell or tissue may have to be ascertained prior to employment of the methods of the invention but such is well within the skill of those in the art and will not be further described in detail herein.

مدر ورود الكوروالية والمدور وود و والموارد والمو

Alternatively, increased expression, such as increased copy number, may be determined for the genes present in a cancerous cell, or a cell suspected of being cancerous, by using the nucleotides sequences as identified in Table 1 as a means of generating probes for the DNAs present in the cells to be examined. Thus, the DNA of such cells may be extracted and probed using the sequences disclosed herein for the presence in the genomes of such cells of increased amounts of one or more of the genes of the invention. For example, where a cancer-related, or cancer-linked, gene as disclosed herein is found to be present in multiple copies within the genome of a cell, even where it may not be actively being over-expressed at the time of such determination, this may be indicative of at least a disposition toward developing cancer at a subsequent time.

25

30

5

10

15

20

In accordance with the foregoing, the presence of such multiple copies of a gene, or genes, as disclosed herein may be determined using northern or southern blotting and employing the sequences as identified in Table 1 to develop probes for this purpose. Such probes may be composed of DNA or RNA and may advantageously be comprised of a contiguous stretch of nucleotide residues matching, or complementary to, a sequence as identified in Table 1. Such probes will most usefully comprise a contiguous stretch of at

least 15, preferably at least 30, more preferably at least 50, most preferably at least 80, and especially at least 100, even 200 residues, derived from one or more of the sequences as identified in Table 1. Thus, where a single probe binds multiple times to the genome of a sample of cells that are cancerous, or are suspected of being cancerous, or predisposed to become cancerous, whereas binding of the same probe to a similar amount of DNA derived from the genome of otherwise non-cancerous cells of the same organ or tissue results in observably less binding, this is indicative of the presence of multiple copies of a gene comprising, or corresponding to, the sequence as identified in Table 1 from which the probe sequenced was derived.

5

10

15

20

25

30

Increased expression may also be determined using agents that selectively bind to, and thereby detect, the presence of expression products of the genes disclosed herein. For example, an antibody, possibly a suitably labeled antibody, such as where the antibody is bound to a fluorescent or radiolabel, may be generated against one of the polypeptides comprising a sequence as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); for polypeptide SEQ ID NOs, see Table 1, serial number 806-923 (transcript or protein)), and said antibody will then react with, binding either selectively or specifically, to a polypeptide encoded by one of the genes that corresponds to a sequence disclosed herein. Such antibody binding, especially relative extent of such binding in samples derived from suspected cancerous, as opposed to otherwise noncancerous, cells and tissues, can then be used as a measure of the extent of expression, or over-expression, of the cancer-related genes identified herein. Thus, the genes identified herein as being over-expressed in cancerous cells and tissues may be over-expressed due to increased copy number, or due to over-transcription, such as where the over-expression is due to overproduction of a transcription factor that activates the gene and leads to repeated binding of RNA polymerase, thereby generating large than normal amounts of RNA transcripts, which are subsequently translated into polypeptides, such as the polypeptides comprising amino acid sequences as

5

10

15

20

25

30

identified in Table 1 (SEQ ID NO: 1-923). Such analysis provides an additional means of ascertaining the expression of the genes identified according to the invention and thereby determining the presence of a cancerous state in a sample derived from a patient to be tested, of the predisposition to develop cancer at a subsequent time in said patient.

In employing the methods of the invention, it should be borne in mind that gene expression indicative of a cancerous state need not be characteristic of every cell found to be cancerous. Thus, the methods disclosed herein are useful for detecting the presence of a cancerous condition within a tissue where less than all cells exhibit the complete pattern of over-expression. For example, a set of selected genes, comprising sequences homologous under stringent conditions, or at least 90%, preferably 95%, identical to at least one of the sequences as identified in Table 1, may be found, using appropriate probes, either DNA or RNA, to be present in as little as 60% of cells derived from a sample of tumorous, or malignant, tissue while being absent from as much as 60% of cells derived from corresponding non-cancerous, or otherwise normal, tissue (and thus being present in as much as 40% of such normal tissue cells). In a preferred embodiment, such gene pattern is found to be present in at least 70% of cells drawn from a cancerous tissue and absent from at least 70% of a corresponding normal, non-cancerous, tissue sample. In an especially preferred embodiment, such gene pattern is found to be present in at least 80% of cells drawn from a cancerous tissue and absent from at least 80% of a corresponding normal, non-cancerous, tissue sample. In a most preferred embodiment, such gene pattern is found to be present in at least 90% of cells drawn from a cancerous tissue and absent from at least 90% of a corresponding normal, noncancerous, tissue sample. In an additional embodiment, such gene pattern is found to be present in at least 100% of cells drawn from a cancerous tissue and absent from at least 100% of a corresponding normal, non-cancerous, tissue sample, although the latter embodiment may represent a rare occurrence.

and of the many control of the second of the

In an additional aspect, the present invention relates to a method for determining a cancer initiating or facilitating gene comprising contacting a cell expressing a test gene (i.e., a gene whose status as a cancer initiating or facilitating gene is to be determined) with an agent that decreases the expression of a gene that encodes an RNA at least 90%, preferably 95%, identical to an RNA encoded by (i.e., a gene corresponding to) a polynucleotide comprising, or having, a sequence selected from the group consisting as identified in Table 1 and detecting a decrease in expression of said test gene compared to when said agent is not present, thereby identifying said test gene as being a cancer initiating or facilitating gene. Such genes may, of course, be oncogenes and said decrease in expression may be due to a decrease in copy number of said gene in said cell or a cell derived from said cell, such as where copy number is reduced in the cells formed by replication of such cells.

Thus, some or all of the genes disclosed herein as corresponding to as identified in Table 1 are found to play a direct role in the initiation or progression of cancer or even other diseases and disease processes. Because changes in expression of these genes (up-regulation) are linked to the disease state (i.e. cancer), the change in expression may contribute to the initiation or progression of the disease. For example, if a gene that is up-regulated is an oncogene such a gene provides for a means of screening for small molecule therapeutics beyond screens based upon expression output alone. For example, genes that display up-regulation in cancer and whose elevated expression contributes to initiation or progression of disease represent targets in screens for small molecules that inhibit or block their function. Examples include, but are not be limited to, kinase inhibition, cellular proliferation, substrate analogs that block the active site of protein targets, etc.

30

25

10

15

20

It should be noted that there are a variety of different contexts in which genes have been evaluated as being involved in the cancerous process.

5

10

15

20

25:

30

Thus, some genes may be oncogenes and encode proteins that are directly involved in the cancerous process and thereby promote the occurrence of cancer in an animal. Other genes may simply be involved either directly or indirectly in the cancerous process or condition and may serve in an ancillary capacity with respect to the cancerous state. All such types of genes are deemed with those to be determined in accordance with the invention as disclosed herein. Thus, the gene determined by said method of the invention may be an oncogene, or the gene determined by said method may be a cancer facilitating gene, the latter including a gene that directly or indirectly affects the cancerous process, either in the promotion of a cancerous condition or in facilitating the progress of cancerous growth or otherwise modulating the growth of cancer cells, either in vivo or ex vivo. Such genes may work indirectly where their expression alters the activity of some other gene or gene expression product that is itself directly involved in initiating or facilitating the progress of a cancerous condition. For example, a gene that encodes a polypeptide, either wild or mutant in type, which polypeptide acts to suppress of tumor suppressor gene, or its expression product, will thereby act indirectly to promote tumor growth.

In accordance with the foregoing, the method of the present invention includes cancer modulating agents that are themselves either polypeptides, or small chemical entities, that affect the cancerous process, including initiation, suppression or facilitation of tumor growth, either *in vivo* or *ex vivo*. Such agents may also be antibodies that react with one or more of the polypeptides as identified in Table 1 ((SEQ ID NO: 806-923 (transcript or protein)).

In keeping with the disclosure herein, the present invention also relates to a method for treating cancer comprising contacting a cancerous cell with an agent having activity against an expression product encoded by a gene mapping within regions of chromosomal interest or, alternatively, a gene corresponding to a polynucleotide that comprises a nucleotide sequence as

identified in Table 1, such as where such expression product is one the polypeptides as identified in Table 1.

The method of the present invention includes embodiments of the above-recited method wherein said cancer cell is contacted *in vivo* as well as *ex vivo*, preferably wherein said agent comprises a portion, or is part of an overall molecular structure, having affinity for said expression product. In one such embodiment, said portion having affinity for said expression product is an antibody.

10

15

20

25

30

5

In one embodiment of the present invention, a chemical agent, such as a protein or other polypeptide, is joined to an agent, such as an antibody, having affinity for an expression product of a cancerous cell, such as a polypeptide or protein encoded by a gene related to the cancerous process, especially a gene sequence corresponding to one of the cDNA sequences as identified in Table 1. In a specific embodiment, said expression product acts as a therapeutic target for the affinity portion of said anticancer agent and where, after binding of the affinity portion of such agent to the expression product, the anti-cancer portion of said agent acts against said expression product so as to neutralize its effects in initiating, facilitating or promoting tumor formation and/or growth. In a separate embodiment of the present invention, binding of the agent to said expression product may, without more, have the effect of deterring cancer promotion, facilitation or growth, especially where the presence of said expression product is related, either intimately or only in an ancillary manner, to the development and growth of a tumor. Thus, where the presence of said expression product is essential to tumor initiation and/or growth, binding of said agent to said expression product will have the effect of negating said tumor promoting activity. In one such embodiment, said agent is an apoptosis-inducing agent that induces cell suicide, thereby killing the cancer cell and halting tumor growth.

Many cancers contain chromosomal rearrangements, which typically represent translocations, amplifications, or deletions of specific regions of genomic DNA. A recurrent chromosomal rearrangement that is associated with a specific stage and type of cancer always affects a gene (or possibly genes) that play a direct and critical role in the initiation or progression of the disease. Many of the known oncogenes or tumor suppressor genes that play direct roles in cancer have either been initially identified based upon their positional cloning from a recurrent chromosomal rearrangement or have been demonstrated to fall within a rearrangement subsequent to their cloning by other methods. In all cases, such genes display amplification at both the level of DNA copy number and at the level of transcriptional expression at the mRNA level.

5

10

15

20

25

30

The present method also relates to a method for determining functionally related genes comprising contacting one or more gene sequences corresponding to the cDNAs as identified in Table 1 with an agent that modulates expression of more than one gene in such group and thereby determining a subset of genes of said group.

In accordance with the present invention, said functionally related genes are genes modulating the same metabolic pathway or said genes are genes encoding functionally related polypeptides. In one such embodiment, said genes are genes whose expression is modulated by the same transcriptional activator or enhancer sequence, especially where said transcriptional activator or enhancer increases, or otherwise modulates, the activity of a gene corresponding to a cDNA as identified in Table 1.

The present invention also relates to a process that comprises a method for producing a product comprising identifying an agent according to one of the disclosed methods for identifying such an agent (i.e., the therapeutic agents identified according to the assay procedures disclosed herein) wherein said product is the data collected with respect to said agent

as a result of said identification process, or assay, and wherein said data is sufficient to convey the chemical character and/or structure and/or properties of said agent. For example, the present invention specifically contemplates a situation whereby a user of an assay of the invention may use the assay to screen for compounds having the desired enzyme modulating activity and having identified the compound, then conveys that information (i.e., information as to structure, dosage, etc) to another user who then utilizes the information to reproduce the agent and administer it for therapeutic or research purposes according to the invention. For example, the user of the assay (user 1) may screen a number of test compounds without knowing the structure or identity of the compounds (such as where a number of code numbers are used the first user is simply given samples labeled with said code numbers) and, after performing the screening process, using one or more assay processes of the present invention, then imparts to a second user (user 2), verbally or in writing or some equivalent fashion, sufficient information to identify the compounds having a particular modulating activity (for example, the code number with the corresponding results). This transmission of information from user 1 to user 2 is specifically contemplated by the present invention.

20

25

30

5

10

15

In accordance with the foregoing, the present invention relates to a method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

- (a) contacting a compound with a cell that expresses at least one gene corresponding to a polynucleotide comprising a nucleotide sequence of serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of SEQ ID NO: 806-923 and under conditions promoting expression of said gene;
- (b) detecting a change in expression of said gene compared to expression when said compound is not present; and
- (c) producing test data with respect to the gene modulating activity of said compound based on a change in the expression of the determined gene,

5

10

15

20

25

30

or genes, whose expression is otherwise elevated in a non-cancerous cell over that in a cancerous cell and a decrease in the expression of the determined gene, or genes whose expression is otherwise increased in a cancerous cell over that in a non-cancerous cell indicating anti-neoplastic activity.

In another embodiment, the present invention provides a method for monitoring the progress of a cancer treatment, such as where the methods of the invention permit a determination that a given course of cancer therapy is or is not proving effective because of an increased or decreased expression of a gene, or genes, disclosed herein. For example, where there is an increased copy number of one or more of the genes as identified in Table 1 (SEQ ID NO: 1-805), monitoring of such genes can predict success or failure of a course of therapy, such as chemotherapy, or predict the likelihood of a relapse based on elevated activity or expression of one or more of these genes following such course of therapy.

In accordance with the foregoing, the present invention contemplates a method for determining the progress of a treatment for cancer in a patient afflicted with cancer, following commencement of a cancer treatment on said patient, comprising:

- (a) determining in said patient a change in expression of one or more genes corresponding to a polynucleotide comprising a nucleotide sequence of serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of serial number 806-923 of Table 1 (which include any of SEQ ID NO: 1 923) and under conditions promoting expression of said one or more genes; and
- (b) detecting a change in expression of said gene compared to expression of said one or more determined genes prior to commencement of said cancer treatment;

thereby determining the progress of said treatment.

5

10

15

20

25

30

In a preferred embodiment, the detected change in expression is a decrease in expression. In another preferred embodiment, the cancer treatment is treatment with a chemotherapeutic agent, especially an agent that modulates, preferably decreases, expression of a gene identified herein, such as where said agent was first identified as having anti-neoplastic activity using a method of the invention. Thus, in accordance with this aspect of the present invention, a patient, or even a research animal, such as a mouse, rat, rabbit or primate, afflicted with cancer, including a cancer induced for research purposes, is introduced to a cancer treatment regimen, such as administration of an anti-cancer agent, including one first identified as having anti-neoplastic activity by one or more of the screening methods disclosed herein. The progress and success or failure of such treatment is subsequently ascertained by determining the subsequent expression of one or more, preferably at least 3, or 5, or 10, of the genes identified herein, or that encodes a transcript or polypeptide disclosed herein (see Table 1) following said treatment. In a preferred embodiment, a treatment that reduces said expression is deemed advantageous and may then be the basis for continuing said treatment. The methods of the invention thereby provide a means of continually monitoring the success of the treatment and evaluating both the need, and desirability, of continuing said treatment. In addition, more than one said treatment may be administered simultaneously without diminishing the value of the methods of the invention in determining the overall success of such combined treatment. Thus, more than one said anti-neoplastic agent may be administered to the same patient and overall effectiveness ascertained by the recited methods.

In accordance with the foregoing, the present invention also contemplates a method for determining the likelihood of survival of a patient afflicted with cancer, following commencement of a cancer treatment on said patient, comprising:

(a) determining in said patient a change in expression of one or more genes corresponding to a polynucleotide comprising a nucleotide sequence of

5

20

25

30

serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of serial number 806-923 of Table 1 and under conditions promoting expression of said one or more genes; and

(b) detecting a change in expression of said gene compared to expression of said one or more determined genes prior to commencement of said cancer treatment;

thereby determining the likelihood of survival of said treatment.

In a preferred embodiment, the detected change in expression is a decrease in expression and said determined gene, or genes, may include 2, 3, 5, 10 or more of the genes described herein. Thus, the methods of the invention may be utilized as a means for compiling cancer survival statistics following one or more, possibly combined, treatments for cancer as in keeping with the other methods disclosed herein.

The genes identified herein also offer themselves as pharmacodynamic markers (or as pharmacogenetic and/or surrogate markers), such as for patient profiling prior to clinical trials and/or targeted therapies, including combination treatments, resulting from the identification of these genes as valid gene targets for chemotherapy based on the screening procedures of the invention. In one embodiment thereof, the likelihood of success of a cancer treatment with a selected chemotherapeutic agent may be based on the fact that such agent has been determined to have expression modulating activity with one or more genes identified herein, especially where said genes have been identified as showing elevated expression levels in samples from a prospective patient afflicted with cancer. Methods described elsewhere herein for determining cancerous status of a cell may find ready use in such evaluations.

It should be cautioned that, in carrying out the procedures of the present invention as disclosed herein, any reference to particular buffers,

media, reagents, cells, culture conditions and the like are not intended to be limiting, but are to be read so as to include all related materials that one of ordinary skill in the art would recognize as being of interest or value in the particular context in which that discussion is presented. For example, it is often possible to substitute one buffer system or culture medium for another and still achieve similar, if not identical, results. Those of skill in the art will have sufficient knowledge of such systems and methodologies so as to be able, without undue experimentation, to make such substitutions as will optimally serve their purposes in using the methods and procedures disclosed herein.

The present invention will now be further described by way of the following non-limiting example. In applying the disclosure of the example, it should be kept clearly in mind that other and different embodiments of the methods disclosed according to the present invention will no doubt suggest themselves to those of skill in the relevant art.

20 EXAMPLE

5

10

15

25

30

Cancerous cells that over-express one or more of the genes selected from those that correspond to genes as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); serial number 806-923 (transcript or protein), or SEQ ID NO: 1 – 805 and 855 - 923) are grown to a density of 10<sup>5</sup> cells/cm² in Leibovitz's L-15 medium supplemented with 2 mM L-glutamine (90%) and 10% fetal bovine serum. The cells are collected after treatment with 0.25% trypsin, 0.02% EDTA at 37°C for 2 to 5 minutes. The trypsinized cells are then diluted with 30 ml growth medium and plated at a density of 50,000 cells per well in a 96 well plate (200 μl/well). The following day, cells are treated with either compound buffer alone, or compound buffer containing a chemical agent to be tested, for 24 hours. The media is then removed, the cells lysed and the RNA recovered

using the RNAeasy reagents and protocol obtained from Qiagen. RNA is quantitated and 10 ng of sample in 1 µl are added to 24 µl of Taqman reaction mix containing 1X PCR buffer, RNAsin, reverse transcriptase, nucleoside triphosphates, amplitaq gold, tween 20, glycerol, bovine serum albumin (BSA) and specific PCR primers and probes for a reference gene (18S RNA) and a test gene (Gene X). Reverse transcription is then carried out at 48°C for 30 minutes. The sample is then applied to a Perlin Elmer 7700 sequence detector and heat denatured for 10 minutes at 95°C. Amplification is performed through 40 cycles using 15 seconds annealing at 60°C followed by a 60 second extension at 72°C and 30 second denaturation at 95°C. Data files are then captured and the data analyzed with the appropriate baseline windows and thresholds.

10

15

20

25 ·

The quantitative difference between the target and reference genes is then calculated and a relative expression value determined for all of the samples used. This procedure is then repeated for each of the target genes in a given signature, or characteristic, set and the relative expression ratios for each pair of genes is determined (i.e., a ratio of expression is determined for each target gene versus each of the other genes for which expression is measured, where each gene's absolute expression is determined relative to the reference gene for each compound, or chemical agent, to be screened). The samples are then scored and ranked according to the degree of alteration of the expression profile in the treated samples relative to the control. The overall expression of the set of genes relative to the controls, as modulated by one chemical agent relative to another, is also ascertained. Chemical agents having the most effect on a given gene, or set of genes, are considered the most anti-neoplastic.

Table 1

Protein/ Transcript			ğ												Se									∢	
Description	hypothetical protein FLJ20354 unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin) CDC20 cell division cycle 20 homolog (S.	cerevisiae)	interferon-stimulated protein 15 kDa	unknown	ESTs	immunoalobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	HSPC150 protein similar to ubiquitin-	conjugating enzyme	similar to rat nuclear ubiquitous casein kinase	confromers profess F 250/4001 /mstrass	Confidence protein r 350/400ka (mitosin)	centiudifiere protein A 17KDa	inconucieotide reductase MZ polypeptide	hypothetical protein FLJ25211	TTK protein kinase	ESTS	KIAA0906 profein	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076
unigene	Hs.133260 NULL	Hs.75616	Hs.69360	Hs.82906	:	Hs.833	NOLL	Hs.133294	Hs.38002	Hs.127310		Hs.234545	Hs.5199		Hs.118064	He 77204	15.7.204 Us 4504	10.134	B1007.8L	HS.44269	Hs.169840	Hs.196042	Hs.56966	Hs.41271	
band	p31.2 p31.3	p32.3	p34.1	p34.2	0	p36.33	q21.3	d22	q23.1	q23.2		q23.3	q32.1	)	q32.1	432.3	2000	750.0 725.1	75. 1	933.1	p21.31	p24.3	p25.1	q12.3	
chr	~ ~	_	_	_	•		_	<del>-</del>	_	τ-		_	_	,	<del>-</del>	~	٠,	1 0	1 0	7	က	က	က	က	
E d	primary primary	primary	primary	primary	-	primary	primary	primary	primary	primary		primary	primary		primary	primary	primary	primary	printary in	primary	primary	primary	primary	primary	
tissue	breast breast	breast	breast	breast	4	DIEGS!	breast	breast	breast	breast		breast	breast		breast	breast	breast	breast	room to	חממאר	breast	breast	breast	breast	
accession	AK000490 R33352	AI739473	U63743	U05340	A A 202242	746444	115144	AI053741	AB037776	AA830844		AF326731	AB032931	70000	AI380204	U30872	U14518	AI492879	AI 045622	70004000	M86699	A1962335	AI867102	AI751438	
SEQ ID	e 19	<u>ა</u>	က	7	7	- 4	<u>y</u> ,	<b>-</b> ;	4,	တ	ı	,	4	o	0	ဖ	55	54	56	3 ;	4 l	: i	ر د	7	
Serial No.	<b>−</b> 0 0	י ני	4	ည	Œ	) [	~ 0	<b>x</b> (	ဘ (	2	•	- 1	72	200	2	4	<del>ن</del>	16	17	- 4	<u>2</u>	<u>n</u>	25	21	

collagen type VIII alpha 1	ESTs Moderately similar to zinc finger protein	91 (HPF7 HTF10) [Homo sapiens] [H.sapiens] epithelial cell transforming sequence 2	oncogene	ESTS	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	inhibin beta A (activin A activin AB alpha	polypeptide)	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	anillin actin binding protein (scraps homolog	Drosophila)	sorting nexin 10	anterior gradient 2 homolog (Xenepus laevis)	enhancer of zeste homolog 2 (Drosophila)	solute carrier family 39 (zinc transporter)	member 4	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	sulfatase FP	tumor protein D52	cyclin E2	mal T-cell differentiation protein 2	hypothetical protein MGC5254	squalene epoxidase
Hs.114599	Hs.36830	Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.727		Hs.28792		Hs.62180		Hs.106260	Hs.91011	Hs.77256	Hs.352415		Hs.67776		Hs.104741	Hs.252587	Hs.70823	Hs.2384	Hs.30464	Hs.76550	Hs.222088	Hs.71465
q12.3	q26.1	q26.32		d28	p13.1	q13.2	g31.1	q31.2	p21.32	p14.1		p14.1	٠	p14.2		p15.2	p21.1	q36.1	NULL		NOLL		p21.1	q13.2	q13.3	q21.13	q22.1	q24.12	q24.13	q24.13
က	က	က		က	2	ည	2	ß	ဖ	7		7		7		/	7	_	∞		ω		∞	ω	ω	∞	œ	∞	∞	ω
primary	primary	primary		primary	primary	primary	primary	primary	primary	primary		primary		primary	•	primary	primary	primary	primary		primary		primary	primary	primary	primary	primary	primary	primary	primary
breast	breast	breast		breast	breast	breast	breast	breast	breast	breast		breast		breast		breast	breast	breast	breast		breast		breast	breast	breast	breast	breast	breast	breast	breast
X57527	W02608	AI823992		AI087975	AW001872	BE407516	U70370	AI739117	D14678	M13436	* 1	AI343467		AK023208		AI285531	AI922323	<b>U61145</b>	AA625199		AI949095		AI932328	AA203476	AW043713	BE974098	AF091433	AA046853	AI925583	AF098865
72	9/	73		78	82	80	81	79	83	82		8	į	84		88	87	88	66		100		0 (	9	92	96	8	92	93	26
22	23	24		22	<b>5</b> 6	27	28	59	30	<del>က</del> ်		32		33	,	34	35	36	37		38		<u>ი</u>	40	41	42	43	44	45	46

Homo sapiens cDNA FLJ14388 fis clone	rizivida 1002/16 zinc finger DHHC domain containing 12	hypothetical protein Fl. 136779	EST	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FL.110540	KIAA0750 gene product	similar to RIKEN cDNA 26100361 13	Serologically defined colon cancer antinen 28	H2A histone family member X	Thy-1 cell surface antiden	forkhead box M1	Rac GTPase activating protein 1	culin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	tubulin beta 4	HSPC037 protein	hypothetical protein MGC4692	selenoprotein X 1	hypothetical protein MGC2605	hypothetical protein El 130003	hypothetical protein MGC2604	Homo sapiens similar to possible G-protein	receptor clone MGC:21993 IMAGE:4398317	ESTs	
Hs.9812	Hs.133122	Hs.212613	Hs.274152	Hs.42650	Hs.334562	Hs.14559	Hs.314434	Hs.23044	Hs.84700	Hs.147097	Hs.125359	Hs.239	Hs.23900	Hs.183874	Hs.84113		Hs. 194698	Hs.81892	Hs.344037	Hs.159154	Hs.108196	Hs.13561	Hs.279623	Hs.124015	Hs 351474	Hs.124915	Hs.290943		Hs.368078	
q24.22	q34.11 <sup>3</sup>	q34.3	q34.3	q21.1	q21.2	q23.33	p15.3	q13.1	q13.4	q23.3	q23.3	p13.33	q13.12	q33.3	q22.1		q21.3	q22.2	q25.3	NOLL	NOLL	p13.3	p13.3	p13.3	p13.3	p13.3	p13.3		q12.2	
<b>©</b>	တ	တ	တ	9	10	9	7	7	7	7	7	12	12	13	14		15	15	15	16	16	16	16	16	16	16	16		16	
primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary		primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary		primary	
breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast		breast	breast		breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast		breast	
AA147884	AW007586	W25552	AI811865	AF067656	AL524035	AI674163	AB018293	AL079372	D60944	X14850	AA704137	U74612	<b>U82984</b>	AI291142	L25876		AL080146	D14657	AA195614	AW003626	BC003186	AI819340	W92110	AI953838	AL520675	BE965311	AI701742		AA904482	
94	103	101	102	17	10	15	21	<u>8</u>	22	10	20	23	<b>5</b> 4	22	<b>5</b> 8	1	/7	<b>5</b>	<b>7</b> 3		32	90	34	32	36	37	ဆွ		33	
47	48	49	20	ર્ગ	25	53	<b>5</b>	55	20	27	23	23	9	61	62	ç	0	<b>4</b> 6	က္က	99	29	89	69 1	2	7	72	73		74	

KIAA1618 protein solute carrier family 16 (monocarboxylic acid transporters) member 3	hypothetical protein BC014072  FSTs Moderately similar to TP2A HIMAN	DNA topoisomerase II alpha isozyme [H.sapiens]	topoisomerase (DNA) II alpha 170kDa	Homo sapiens Similar to epsin 3 clone	MGC:1006 IMAGE:3505495 mRNA complete cds	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens]	TO A COLOR OF THE COLOR	i RACHZU10824 nigniy similar to Riboni cleoprofein	hypothetical protein MGC11138	karyopherin alpha 2 (RAG cohort 1 importin	alpha 1)	hematological and neurological expressed 1	thymidine kinase 1 soluble	highly expressed in cancer rich in leucine	heptad repeats	ubiquitin UBF-fl	KIAA0186 gene product	retinoic acid induced 3	chromosome 20 open reading frame 1		ubiquitin-conjugating enzyme E2C	ribosomal protein L4	breast carcinoma amplified sequence 4	
Hs.314169 Hs.85838	Hs.348504 Hs.370428		Hs.156346	Hs.307036		Hs.165909	Us 402542	118, 1030 12		Hs.90207	Hs.159557		Hs.109706	Hs.105097	Hs.58169		Hs.288549	Hs.36232	Hs.194691	Hs.9329	Hs.274411	Hs.93002	Hs.286	Hs.56237	
NOLL NULL	911.2	- - - - - - -	q21.31	q2.3 q		q23.2	422.2	450.5		q24.2	q24.3		q25.3	q25.3	p11.32		q13.43	p11.21	p11.23	q11.1	q11.22	q13.12	q13.12	q13.13	
14	7 2	:	77	17		17	17	=		17	17		17	17	<u>8</u>		<del>0</del>	20	20	20	20	20	20	20	
primary primary	primary primary		primary	primary		primary	nriman,	ر الا الا الا الا الا الا الا الا الا ال		primary	primary		primary	primary	primary		primary	primary	primary	primary	primary	primary	primary	primary	
breast breast	breast breast	. ·	breast breast	breast		breast	hreact	ol cast		breast	breast		breast	breast	breast		breast	breast	breast	breast	breast	breast	breast	breast	
AI683036 U81800	BE328850 AW003286		AL561834 I 47276	BC001038		AA424160	RE029215	2000		AI675178	U28386		AA635844	K02581	AF017790		AA719022	D80008	A1990405	AA534688	AW003586	U73379	A1990026	AA207074	
44 44	45 39		4 1 1 8	49		9	5.	5		43	20	,	46 i	47	25	í	53	65	63	22	99	29	62	29	
75 76	77		6 80 80	81		82	83	}		84	82		တ္ထ မ	87	ထ္ထ	9	က ဇ	၁၈	91	92	က္တ	94	92	96	

breast carcinoma amplified sequence 1		•	KINA eukarvotic translation elongation factor 1 alpha	2	collagen type I alpha 1		reticulum protein retention receptor 3			unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin)	CDC20 cell division cycle 20 homolog (S.	cerevisiae)	microfibrillar-associated protein 2	interferon-stimulated protein 15 kDa	unknown				gene (stathmin)	nnknown			ESTS	HSPC150 protein similar to ubiquitin-	conjugating enzyme	similar to rat nuclear ubiquitous casein kinase	
Hs.129057	Hs.250822	Hs.83883	Hs.2642		Hs.172928	Hs.250696		Hs.208912	Hs.133260	NULL	Hs.75616	Hs.69360		Hs.82906		Hs.83551	Hs.833	NOLL	Hs. 133294	Hs.38002	Hs.127310		NOLL	Hs.234545	Hs.191187	Hs.209609	Hs.5199		Hs.118064	
q13.2	q13.31	q13.32	q13.33		q13.1	q13.1		q13.2	p31.2	p31.3	p32.3	p34.1		p34.2		p36.13	p36.33	q21.3	g22	q23.1	q23.2		q23.2	q23.3	q23.3	q25.2	q32.1		q32.1	
20	20	20	20		22	22		22	_	<del>-</del>	<del>-</del>	<del></del>		<del></del>		<del>-</del>	~	~	τ	_	~		τ-	<del>-</del>	<u>_</u>	<del></del>	~		<del>-</del>	
primary	primary	primary	primary		primary	primary		primary	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	
breast	breast	breast	breast		breast	breast		breast	breast	breast	breast	breast		breast		breast	breast	breast	breast	breast	breast		breast	breast	breast	breast	breast		breast	
AF041260	AF011468	AA535819	X70940		Y15915	AL035081		Al381686	AK000490	R33352	AI739473	U63743		U05340		A1992172	AA203213	T16144	AI053741	AB037776	AA830844		K62346	AF326731	AI983896	AI798144	A1990409		A1380204	
00 7	61	28	64		69	9	(	89	106	113	116	108	1	105	7	3.13	114	115	104	118	112	9	120	110	117	121	107			
97	သ ်	66	100		101	102		103	104	105	106	107	0	108	2	<u> </u>	110	111	112	113	114		<u>Ω</u>	116	117	118	119	,	071	

centromere protein F 350/400ka (mitosin)	centromere protein A 17kDa	ribonucleotide reductase M2 polypeptide	hypothetical protein FLJ25211	hairy and enhancer of split 6 (Drosophila)	TTK protein kinase	unknown	ESTs	KIAA0906 protein	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076	collagen type VIII alpha 1	ESTs Moderately similar to zinc finger protein	91 (HPF7 HTF10) [Homo sapiens] [H.sapiens]	ESTs	epithelial cell transforming sequence 2	oncogene	ESTS	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	inhibin beta A (activin A activin AB alpha	polypeptide)	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	anillin actin binding protein (scraps homolog	Drosophila)	Homo sapiens Similar to RIKEN cDNA	E130201N16 gene clone IMAGE:3845782
Hs.77204	Hs.1594	Hs.75319	Hs.44269	Hs.42949	Hs.169840	NOLL	Hs.196042	Hs.56966	Hs.41271		Hs.114599	Hs.36830		Hs.128773	Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.727		Hs.28792		Hs.62180		Hs.91109	
q32.3	p23.3	p25.1	q33.1	q37.3	p21.31	p21.31	p24.3	p25.1	q12.3		q12.3	q26.1		q26.31	q26.32		d28	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1		p14.1		p14.2		p15.1	
_	7	7	~	~	ო	က	က	က	က		က	က		က	က		က	ည	ည	ß	S.	9	7		^		7		7	
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic		metastatic	
breast	breast	breast	breast	breast	breast	breast	breast	breast	breast		breast	breast		breast	breast		breast	breast	breast	breast	breast	breast	breast		breast		breast		breast	
U30872	<b>U14518</b>	AI492879	AL045632	N21131	M86699	AA663786	A1962335	AB020713	AI557210		X57527	W02608		AI760298	AI823992		AI087975	AW001872	N90191	U70370	AI739117	D14678	M13436		AA059458		AK023208		AI742239	
109	169	168	170	171	191	197	194	195	188		189	192		193	190		196	201	199	200	198	202	204		205		203		211	
121	122	123	124	125	126	127	128	129	130		131	132		133	134		135	136	137	138	139	140	141		142		143		144	

mRNA

sorting nexin 10	anterior gradient 2 homolog (Xenepus laevis)	collagen type I alpha 2	polymerase (RNA) II (DNA directed)	polypeptide J 13.3kDa	enhancer of zeste homolog 2 (Drosophila)	solute carrier family 39 (zinc transporter)	member 4	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	cellular retinoic acid binding protein 1	kinesin family member C2-like	rhophilin 1	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	sulfatase FP	tumor protein D52	cyclin E2	ESTs	mal T-cell differentiation protein 2	hypothetical protein MGC5254	squalene epoxidase	Homo sapiens cDNA FLJ14388 fis clone	HEMBA1002716	zinc finger DHHC domain containing 12	hypothetical protein FLJ36779	EST	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	kinesin-like 1	Homo sapiens cDNA FLJ32525 fis clone	
Hs.106260	Hs.91011	Hs.179573	Hs.80475		Hs.77256	Hs.352415		Hs.67776		Hs.346950	Hs.92679	Hs.149152	Hs.104741	Hs.252587	Hs.70823	Hs.2384	Hs.30464	Hs.162697	Hs.76550	Hs.222088	Hs.71465	Hs.9812		Hs.133122	Hs.212613	Hs.274152	- Hs.42650	Hs.334562	Hs.14559	Hs.8878	Hs.185918	
p15.2	p21.1	q21.3	q22.1		q36.1	NULL		NOLL		NOLL	NULL	NOLL	p21.1	q13.2	q13.3	q21.13	q22.1	q24.11	q24.12	q24.13	q24.13	q24.22		q34.11	q34.3	q34.3	q21.1	q21.2	q23.33	q23.33	p15.1	
7	/	/	7		/	ω		ω		ω	ω	∞	ω	ω	ω	∞	∞	<b>ω</b>	ω	ω	∞	∞ .		တ	တ	တ	9	9	9	9	7	
metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	
breast	breast	breast	breast		breast	breast		breast		breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast		breast	breast	breast	breast	breast	breast	breast	breast	
AI285531	AI922323	AI961907	L37127		<b>U61145</b>	AA625199		A1949095		W22510	AA292431	AI917311	A1932328	AA203476	BE500977	BE974098	AF091433	AA610522	AA046853	AI656807	D78130	AA147884		AW007586	W25552	AI811865	AF067656	D88357	AI674163	<b>U37426</b>	AA705015	
208	206	209	210		207	220		223		224	225	226	212	213	215	217	219	222	216	218	221	214		229	227	228	124	123	122	125	131	
145	146	147	148		149	150		151		152	153	154	155	156	157	158	159	160	161	162	163	164		165	166	167	168	169	170	171	172	

SMINT2000060	KIAA0750 gene product similar to RIKEN cDNA 2610036L13	serologically defined colon cancer antigen 28	H2A histone family member X	Thy-1 cell surface antigen	forkhead box M1	Rac GTPase activating protein 1	Human clone 295 5cM region surrounding	hepatocyte nuclear factor-1a/MODY3 mRNA	cullin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	tubulin beta 4	HSPC037 protein	Homo sapiens cDNA FLJ14059 fis clone	HEMBB1000573	ESTs Highly similar to hypothetical protein FLJ13593 [Homo sapiens] [H.sapiens]	hypothetical protein MGC4692	selenoprotein X 1	hypothetical protein MGC2605	hypothetical protein FLJ30002	hypothetical protein MGC2601	Homo sapiens similar to possible G-protein	receptor clone MGC:21993 IMAGE:4398317 mRNA complete cds	serine/arginine repetitive matrix 2	ESTs
	Hs.314434 Hs.23044	Hs.84700	Hs.147097	Hs.125359	Hs.239	Hs.23900	Hs.204166		Hs.183874	Hs.84113		Hs.194698	Hs.81892	Hs.344037	Hs.159154	Hs.108196	Hs.289047		Hs.115838	Hs.13561	Hs.279623	Hs.124015	Hs.351474	Hs.124915	Hs.290943		Hs.197114	Hs.368078
	p15.3 q13.1	q13.4	q23.3	q23.3	p13.33	q13.12	q24.31		q33.3	q22.1		q21.3	q22.2	q25.3	NOLL	NOLL	p12.3		p12.3	p13.3	p13.3	p13.3	p13.3	p13.3	p13.3		p13.3	q12.2
	<del>=</del> <del>=</del> = =	7	7	7	12	12	12		<del>1</del> 3	4		15	15	15	16	16	16		9	9	16	16	16	9	16		16	16
	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic
	breast breast	breast	breast	breast	breast	breast	breast		breast	breast		breast	breast	breast	breast	breast	breast		breast	breast	breast	breast	breast	breast	breast		breast	breast
	AB018293 AL079372	AF151810	X14850	AA704137	U74612	U82984	R61322		AI291142	L25876	F	AL080146	D14657	AA195614	AW003626	BC003186	AI766311		Al344053	AI819340	W92110	A1953838	AL520675	BE965311	AI701742		AI655799	AA904482
	129 126	130	127	128	132	133	134		135	136		137	138	139	141	142	149		151	140	144	145	146	147	148		150	143
	173	175	176	177	178	179	180		181	182		183	184	185	186	187	188		189	190	191	192	193	194	195	-	196	197

KIAA1618 protein solute carrier family 16 (monocarboxylic acid transporters) member 3	hypothetical protein BC014072 ESTs Moderately similar to TP2A_HUMAN DNA topoisomerase II alpha isozyme	[H.sapiens] topoisomerase (DNA) II alpha 170kDa unknown	Homo sapiens Similar to epsin 3 clone MGC:1006 IMAGE:3505495 mRNA complete cds	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]	Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to Ribonucleoprotein	hypothetical protein MGC11138	karyopherin alpha 2 (หAG cohort 1 importin alpha 1)	ESTs	thymidine kinase 1 soluble	hematological and neurological expressed 1	highly expressed in cancer rich in leucine heptad repeats	ubiquitin ÚBF-fl	KIAA0186 gene product	retinoic acid induced 3	chromosome 20 open reading frame 1	SCAN domain containing 1	ubiquitin-conjugating enzyme E2C	ribosomal protein L4
Hs.314169 Hs.85838	Hs.348504 Hs.370428	Hs.156346 NULL	Hs.307036	Hs.165909	Hs.103512	Hs.90207	Hs. 15955/	Hs.42645	Hs.105097	Hs.109706	Hs.58169	Hs.288549	Hs.36232	Hs.194691	Hs.9329	Hs.274411	Hs.93002	Hs.286
NULL	q11.2 q21.31	q21.31 q21.31	d22	q23.2	q23.2	q24.2	q24.3	q24.3	q25.3	q25.3	p11.32	q13.43	p11.21	p11.23	q11.1	q11.22	q13.12	q13.12
17	17	77	17	17	7	14	1	17	17	17	<del>2</del>	<del>0</del>	20	20	50	20	20	20
metastatic metastatic	metastatic metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
breast breast	breast breast	breast breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast
AI683036 U81800	BE328850 AW003286	AI375913 L47276	BC001038	AA424160	BF029215	AI675178	028386	N42752	K02581	AI525822	AF017790	AA719022	D80008	A1990405	AF098158	AW003586	U73379	A1990026
154 156	157 152	158 161	162	153	164	155	163	165	159	160	166	167	180	178	177	181	173	176
198	200	202 203	204	205	206	207	802	209	210	211	212	213	214	215	216	217	218	219

breast carcinoma amplified sequence 4	breast carcinoma amplified sequence 1	sal-like 4 (Drosophila)	serine/threonine kinase 6	transmembrane prostate androgen induced RNA	eukaryotic translation elongation factor 1 alpha	2	ESTs	collagen type I alpha 1	KDEL (Lys-Asp-Glu-Leu) endoplasmic	reticulum protein retention receptor 3	hypothetical protein MGC861	hypothetical protein FLJ20354	unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin)	CDC20 cell division cycle 20 homolog (S.	cerevisiae)	ribosomal protein L4	unknown	ESTs	immunoglobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	similar to rat nuclear ubiquitous casein kinase	2	HSPC150 protein similar to ubiquitin-	conjugating enzyme centromere protein F 350/400ka (mitosin)
Hs.56237	Hs.129057	Hs.189095	Hs.250822	Hs.83883	Hs.2642		Hs.224895	Hs.172928	Hs.250696		Hs.208912	Hs.133260	NOLL	Hs.75616	Hs.69360		Hs.82906		Hs.286	NOLL	Hs.133294	Hs.38002	Hs.127310		Hs.234545	Hs.118064		Hs.5199	Hs.77204
q13.13	q13.2	q13.2	q13.31	q13.32	q13.33	-	q13.33	q13.1	q13.1		q13.2	p31.2	p31.3	p32.3	p34.1		p34.2		p35.3	q21.3	d22	q23.1	q23.2		q23.3	q32.1		q32.1	q32.3
20	20	20	20	20	20		20	22	22		22	<del>-</del>	<del>-</del>	<del>-</del>	<del>-</del>		~		<del>-</del>	<del>-</del>	<del>-</del>	<del></del>	<del>-</del>		<del>-</del>	<del>-</del>		<del>-</del>	<b>←</b>
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic		metastatic	primary	primary	primary	primary	•	primary		primary	primary	primary	primary	primary		primary	primary		primary	primary
breast	breast	breast	breast	breast	breast		breast	breast	breast		breast	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon		colon	colon		colon	colon
AA207074	AF041260	A1638036	AF011468	AA535819	X70940		AI872267	Y15915	AL035081		AI961206	AK000490	R33352	AI739473	U63743		<b>U05340</b>		A1990026	T16144	AW271106	AB037776	AA830844		AA383718	AI380204		A1990409	U30872
182	174	183	175	172	179		184	186	187		185	241	235	233	239		243		242	234	232	230	236		231	237		240	238
220	221	222	223	224	225		226	227	228		229	230	231	232	233		234		235	236	237	238	239		240	241		242	243

centromere protein A 17kDa	ribonucleotide reductase M2 polypeptide	hypothetical protein FLJ25211	TTK protein kinase	ESTS	KIAA0906 protein	collagen type VIII alpha 1	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076	epithelial cell transforming sequence 2	oncogene	ESTs	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	inhibin beta A (activin A activin AB alpha	polypeptide)	anillin actin binding protein (scraps homolog	Drosophila)	anterior gradient 2 homolog (Xenepus laevis)	enhancer of zeste homolog 2 (Drosophila)	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	solute carrier family 39 (zinc transporter)	The Management of the state of	I -LAK cell-originated protein kinase	promedy correctional solutions of the so	sulfatase FP
Hs.1594	Hs.75319	Hs.44269	Hs.169840	Hs.196042	Hs.56966	Hs.114599	Hs.41271		Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.28792		Hs.727		Hs.62180		Hs.91011	Hs.77256	Hs.67776		Hs.352415	112 404744	HS.104/41	118.232307	US. / U023
p23.3	p25.1	q33.1	p21.31	p24.3	p25.1	q12.3	q12.3		q26.32		d58	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1		p14.1		p14.2		p21.1	q36.1	NOLL	-	NOLL	7 70	p21.1	4.0.4	q13.3
7	7	7	က	ო	က	က	က		က		က	ည	2	വ	ည	ဖ	7		^		7		_	_	∞		∞	c	οα	0	o <sub>.</sub>
primary	primary	primary	primary	primary	primary	primary	primary		primary		primary	primary	primary	primary	primary	primary	primary		primary		primary		primary	primary	primary		primary		primary primary	primary	pilliary
colon	colon	colon	colon	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon	colon	colon		colon		colon		colon	colon	colon		colon	100			
U14518	BE966236	AL045632	M86699	A1962335	AB020713	X57527	AI557210		AI823992		AI087975	AW001872	M25753	U70370	AI739117	D14678	AA059458		M13436		AI341261		A1922323	U61145	AI949095		AA625199	ALCOCOLA	A1932326 AA203476	AN(A9742	AVV0457 15
284	285	283	302	301	300	304	305		. 303			307			309	310	313		315		314		312	311	316		318	300	327	525	223
244	245	246	247	248	249	250	251		252		253	254	255	256	257	258	259		260		261		262	263	264		265	900	267	780	007

cyclin E2	mal T-cell differentiation protein 2	squalene epoxidase	hypothetical protein MGC5254	Homo sapiens cDNA FLJ14388 fis clone	HEINIBA I UUZ / 10	zinc finger DHHC domain containing 12	EST	hypothetical protein FLJ36779	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	KIAA0750 gene product	similar to RIKEN cDNA 2610036L13	serologically defined colon cancer antigen 28	Thy-1 cell surface antigen	H2A histone family member X	forkhead box M1	Rac GTPase activating protein 1	cullin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	HSPC037 protein	tubulin beta 4	Homo sapiens similar to possible G-protein	receptor clone MGC:21993 IMAGE:4398317 mRNA complete cds	hypothetical protein MGC2601	hypothetical protein FLJ30002	
Hs.30464	Hs.76550	Hs.71465	Hs.222088	Hs.9812		Hs.133122	Hs.274152	Hs.212613	Hs.42650	Hs.334562	Hs.14559	Hs.314434	Hs.23044	Hs.84700	Hs.125359	Hs.147097	Hs.239	Hs.23900	Hs.183874	Hs.84113		Hs.194698	Hs.81892	Hs.344037	Hs.108196	Hs.159154	Hs.290943		Hs.124915	Hs.351474	
q22.1	q24.12	q24.13	q24.13	q24.22		q34.11	q34.3	q34.3	q21.1	q21.2	q23.33	p15.3	q13.1	q13.4	q23.3	q23.3	p13.33	q13.12	q33.3	q22.1		q21.3	q22.2	q25.3	NOLL	NULL	p13.3		p13.3	p13.3	
∞	ω	ω	∞	ω		တ	တ	တ	10	9	9	7	7	7	7	7	12	12	13	4		15	15	15	16	16	16		16	10	
primary	primary	primary	primary	primary		primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary	primary		primary	primary	primary	primary	primary	primary	-	primary	primary	
colon	colon	colon	colon	colon		colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon	colon		colon	colon	coloo	colon	colon	colon		colon	colon	
AF091433	AL117612	D78130	AI656807	AA147884		AW007586	AI811865	W25552	AF067656	AL524035	AI674163	AB018293	AL079372	D60944	AA704137	X14850	U74612	U82984	AI291142	L25876		AL080146	D14657	AA195614	BC003186	AW003626	AI701742		RE965311	AL520675	
319	321	317	320	322		326	327	328	244	245	246	248	251	247	249	250	253	252	254	255		258	257	256	265	266	259		260	261	
569	270	271	272	273		274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	) 	289	290	291	292	293	294		295	296	

Table 1 (Continued)

hypothetical protein MGC2605	selenoprotein X 1	hypothetical protein MGC4692	2	solute carrier family 16 (monocarboxylic acid	noer	KIAA1618 protein	hypothetical protein BC014072	unknown	topoisomerase (DNA) II alpha 170kDa	ESTs Moderately similar to TP2A_HUMAN	DNA topoisomerase II alpha isozyme [H.sapiens]	Homo sapiens Similar to epsin 3 clone	MGC:1006 IMAGE:3505495 mRNA complete		Homo sapiens cDNA FLJ36569 fis clone	TRACH2010824 highly similar to	Ribonucleoprotein	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens]	hypothetical protein MGC11138	karyopherin alpha 2 (RAG cohort 1 importin	alpha 1)	hematological and neurological expressed 1	thymidine kinase 1 soluble	highly expressed in cancer rich in leucine	heptad repeats	ubiquitin UBF-fl	KIAA0186 gene product	retinoic acid induced 3	chromosome 20 open reading frame 1
hypo	sele	hypu	ESTs	solu	ıran	₹	hyp	u S	topc	EST	H.S.E.	문	ğ.	Spo	된	TR	Rigo	EST	Ę	hyp	kary	흡	hen	thy	high	hep	nbign	₹ Y	retir	chro
Hs.124015	Hs.279623	Hs.13561	Hs.368078	Hs.85838		Hs.314169	Hs.348504	NOLL	Hs.156346	Hs.370428		Hs.307036			Hs.103512			Hs.165909		Hs.90207	Hs.159557		Hs.109706	Hs.105097	Hs.58169		Hs.288549	Hs.36232	Hs.194691	Hs.9329
p13.3	p13.3	p13.3	q12.2	NOLL		NOLL	q11.2	q21.31	q21.31	q21.31		q22			q23.2			q23.2		q24.2	q24.3		q25.3	q25.3	p11.32		q13.43	p11.21	p11.23	q11.1
16	16	16	9	17	!	17	17	17	17	. 4		17			17			17		17	17		17	1	<del>2</del>		9	20	20	20
primary	primary	primary	primary	primary		primary	primary	primary	primary	primary		primary			primary			primary		primary	primary	•	primary	primary	primary		primary	primary	primary	primary
colon	colon	colon	colon	colon		colon	colon	colon	colon	colon		colon			colon	÷		colon		colon	colon		colon	colon	colon		colon	colon	colon	colon
A1953838	W92110	AI819340	AA904482	U81800		AI683036	BE328850	L47276	AI375913	AW003286		BC001038			BF029215			BG165011		AI675178	U28386		AI525822	K02581	AF017790		AA719022	D80008	A1990405	AF098158
262	263	267	264	276		278	275	272	274	280		271			269			279		277	270		268	273	281		282	288	290	291
297	298	299	300	301		302	303	304	305	306		307			308			308		310	311		312	313	314		315	316	317	318

SCAN domain containing 1	ubiquitin-conjugating enzyme E2C	breast carcinoma amplified sequence 4	breast carcinoma amplified sequence 1	serine/threonine kinase 6	transmembrane prostate androgen induced	KINA	eukaryotic transiation elongation factor 1 alpha 2	VDEL (Live Aca Chill on) endenlasmic	NDEL (Lys-Asp-Glu-Leu) alluopiasiilio reticulum protein retention receptor 3		conagen type I aipila 1	hypothetical protein MGC861	hypothetical protein FLJ20354	unknown	24-dehydrocholesterol reductase	kinesin-like 6 (mitotic centromere-associated	kinesin) ,	CDC20 cell division cycle 20 homolog (S.	cerevisiae)	ribosomal protein L4	unknown	ESTs	immunoglobulin superfamily member 9	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	ESTs	cell division cycle associated 1	similar to rat nuclear ubiquitous casein kinase	2	· HSPC150 protein similar to ubiquitin-
Hs.274411	Hs.93002	Hs.56237	Hs.129057	Hs.250822	Hs.83883		HS.2642	202020	US.250090	110 470000	US.11.2920	Hs.208912	Hs.133260	NULL	Hs.75616	Hs.69360		Hs.82906		Hs.286	NULL	Hs.133294	Hs.38002	Hs.127310		Hs.234545	Hs.191187	Hs.234545	Hs.118064		Hs.5199
q11.22	q13.12	q13.13	q13.2	q13.31	q13.32		q13.33	7 0 7 1	d :5: -	7 077	ط-5. <del>ا</del>	q13.2	p31.2	p31.3	p32.3	p34.1		p34.2		p35.3	q21.3	d22	q23.1	q23.2		q23.3	q23.3	q23.3	q32.1		q32.1
20	20	20	20	20	20	- 1	20	ç	77	ç	77	22	<del>-</del>	<del>-</del>	_	~		_		_	_	<del>-</del>	_	_		<del>-</del>	_	<del>-</del>	<del>-</del>		<del></del>
primary	primary	primary	primary	primary	primary		primary	•	primary		primary	primary	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic
colon	colon	colon	colon	colon	colon		colon		COIOD		COOO	colon	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon		colon	colon	colon	colon		colon
AW003586	U73379	AA207074	AF041260	AF011468	AA535819		X70940	700100	ALU35081	0701	Y15916	AI381686	AK000490	R33352	AI739473	U63743	•	U05340		AI990026	T16144	AW271106	AB037776	AA830844		AF326731	AI983896	AF326731	AI380204		Al990409
287	294	286	293	292	295		289	0	296	100	787	298	420	354	351	396		425		421	352	346	340	357		330	341	380	360		403
319	320	321	322	.323	324		325	9	326	100	32/	328	329	330	331	332	† !	333		334	335	336	337	338		336	340	341	342		343

Table 1 (Continued)

conjugating enzyme	centromere protein F 350/400ka (mitosin)	centromere protein A 17kDa	ribonucleotide reductase M2 polypeptide	hypothetical protein FLJ25211	TTK protein kinase	ESTs	KIAA0906 protein	collagen type VIII alpha 1	Homo sapiens mRNA full length insert cDNA	clone EUROIMAGE 1913076	ESTs Moderately similar to zinc finger protein 91 (HPF7 HTF10) [Homo sapiens] [H sapiens]	epithelial cell transforming sequence 2	oucogene	ESTS	FYN binding protein (FYB-120/130)	cyclin B1	paired-like homeodomain transcription factor 1	RAB6 interacting kinesin-like (rabkinesin6)	kinesin-like 2	Homo sapiens cDNA FLJ11041 fis clone	PLACE1004405	Homo sapiens cDNA FLJ11041 fis clone PLACE1004405	inhibin beta A (activin A activin AB alpha	polypeptide)	anillin actin binding protein (scraps homolog Drosophila)	anillin actin binding protein (scraps homolog	anillin actin binding protein (scraps homolog	
	Hs.77204	Hs.1594	Hs.75319	Hs.44269	Hs.169840	Hs.196042	Hs.56966	Hs.114599	Hs.41271		Hs.36830	Hs.122579		Hs.195225	Hs.58435	Hs.23960	Hs.84136	Hs.73625	Hs.20830	Hs.28792		Hs.28792	Hs.727		Hs.62180	Hs.62180	Hs.62180	
	q32.3	p23.3	p25.1	<b>q33.1</b>	p21.31	p24.3	p25.1	q12.3	q12.3		q26.1	q26.32		d28	p13.1	q13.2	q31.1	q31.2	p21.32	p14.1		p14.1	p14.1		p14.2	p14.2	p14.2	
	~	7	7	~	က	က	က	ო	က		က	ო		က	ည	ည	വ	S.	ဖ	7		^	7		7	7	7	
	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	
	colon	colon	colon	colon	uoloo .	colon	colon	colon	colon		colon	colon		colon	colon	colon	colon	coloo	colon	colon		colon	colon		colon	colon	colon	
	U30872	<b>U14518</b>	BE966236	AL045632	M86699	A1962335	AB020713	X57527	AI557210		W02608	AI823992		AI087975	AW001872	M25753	U70370	AI739117	D14678	AA059458		AI343467	M13436		AK023208	AK023208	AK023208	
	382	400	419	349	365	334	333	412	417		344	395		332	409	408	410	434	389	427		436	437		329	438	440	
	344	345	346	347	348	349	350	351	352		353	354		355	356	357	358	359	360	361		362	363		364	365	366	

Drosophila)	sorting nexin 10	anterior gradient 2 homolog (Xenepus laevis)	collagen type I alpha 2	enhancer of zeste homolog 2 (Drosophila)	Homo sapiens clone IMAGE:5455669 mRNA	partial cds	solute carrier family 39 (zinc transporter)	member 4	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	sulfatase FP	tumor protein D52	cyclin E2	ESTs	mal T-cell differentiation protein 2	squalene epoxidase		Homo sapiens cDNA FLJ14388 fis clone	HEMBA1002716			hypothetical protein FLJ36779	ZW10 interactor	_	hypothetical protein FLJ10540				similar to RIKEN cDNA 2610036L13	••	Thy-1 cell surface antigen
	Hs.106260	Hs.91011	Hs.179573	Hs.77256	Hs.67776		Hs.352415		Hs.104741	Hs.252587	Hs.70823	Hs.2384	Hs.30464	Hs.162697	Hs.76550	Hs.71465	Hs.222088	Hs.9812		Hs.133122	Hs.274152	Hs.212613	Hs.42650	Hs.334562	Hs.14559	Hs.185918	707770	10.0 14404	Hs.23044	Hs.84700	Hs.125359
	p15.2	p21.1	q21.3	q36.1	NULL		NULL		p21.1	q13.2	q13.3	q21.13	q22.1	q24.11	q24.12	q24.13	q24.13	q24.22	-	q34.11	q34.3	q34.3	q21.1	q21.2	q23.33	p15.1		0.01d	q13.1	q13.4	q23.3
	7	7	7	7	∞		ω		ω	ω	∞	∞	ω	ω	ω	ω	∞	∞		ග	တ	တ	9	9	9	7	;		<del></del>	7	7
	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic
	colon	colon	colon	colon	colon		colon		colon	colon	colon	colon	colon	colon	colon	colon	colon	coloo		colon	colon	colon	colon	colon	colon	colon	-	COIOD	colon	colon	colon
	AI285531	AI922323	A1961907	U61145	A1949095		AA625199		AI932328	AA203476	AW043713	AA524023	AF091433	AA610522	AL117612	D78130	AI656807	AA147884		AW007586	AI811865	W25552	AF067656	X05360	AI674163	AA705015		AB018283	AL079372	D60944	AA704137
	348	392	339	356	336		362		439	428	414	345	363	342	373	347	366	388		374	383	393	355	368	416	337	į	3/7	401	350	379
•	367	368	369	370	371		372		373	374	375	376	377	378	379	380	381	382		383	384	385	386	387	388	389	6	390	391	392	393

Table 1 (Continued)

H2A histone family member X	forkhead box M1	Rac GTPase activating protein 1	Human clone 295 5cM region surrounding	hepatocyte nuclear factor-1a/MODY3 mRNA	cullin 4A	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	cyclin B2	KIAA0101 gene product	protein regulator of cytokinesis 1	HSPC037 protein	tubulin beta 4	Homo sapiens similar to possible G-protein	receptor clone MGC:21993 IMAGE:4398317	mRNA complete cds	hypothetical protein MGC2601	hypothetical protein FLJ30002	hypothetical protein MGC2605	selenoprotein X 1	hypothetical protein MGC4692	ESTs .	solute carrier family 16 (monocarboxylic acid	transporters) member 3	KIAA1618 protein	hypothetical protein BC014072	unknown	topoisomerase (DNA) II alpha 170kDa	ESTs Moderately similar to TP2A_HUMAN	DNA topoisomerase II alpha isozyme	in sapierisj Homo sapiens Similar to epsin 3 clone
Hs.147097	Hs.239	Hs.23900	Hs.204166		HS.183874	Hs.84113		Hs.194698	Hs.81892	Hs.344037	Hs.108196	Hs.159154	Hs.290943			Hs.124915	Hs.351474	Hs.124015	Hs.279623	Hs.13561	Hs.368078	Hs.85838		Hs.314169	Hs.348504	NOLL	Hs.156346	Hs.370428		Hs.307036
q23.3	p13.33	q13.12	q24.31	0	933.3	q22.1		q21.3	q22.2	q25.3	NOLL	NOLL	p13.3			p13.3	p13.3	p13.3	p13.3	p13.3	q12.2	NOLL		NOLL	q11.2	q21.31	q21.31	q21.31		q22
7	7	12	12	,	13	4		<del>1</del> 2	15	15	16	16	16			16	16	9	9	16	16	17		17	17	17	17	17		17
metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic			metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic
colon	colon	colon	colon	10100	U000	colon		colon	colon	colon	colon	colon	colon			colon	colon	colon	colon	colon	colon	colon		colon	colon	colon	colon	colon		colon
X14850	<b>U74612</b>	U82984	R61322	07770014	AI291142	L25876		AL080146	D14657	AA195614	BC003186	AW003626	AI701742			BE965311	AL520675	A1953838	W92110	AI819340	AA904482	U81800		AI683036	BE328850	L47276	AI375913	AW003286		BC001038
381	429	384	343	252	000	387	(	423	413	406	407	415	358			361	364	377	385	431	405	391		411	390	376	386	432		375
394	395	396	397	300	000	366		400	401	402	403	404	405			406	407	408	409	410	411	412		413	414	415	416	417		418

MGC:1006 IMAGE:3505495 mRNA complete					·	highly expressed in cancer rich in leucine heptad repeats			_	retinoic acid induced 3	_			breast carcinoma amplified sequence				KINA eukaryotic translation elongation factor 1 alpha 2	6 KDEL (Lys-Asp-Glu-Leu) endoplasmic reficulum protein retention receptor 3	
	Hs.103512	Hs.165909	Hs.90207 Hs.159557	Hs.109706	Hs.105097	Hs.58169	Hs.58169	Hs.288549	Hs.36232	Hs.194691	Hs.9329	Hs.274411	Hs.93002	Hs.56237	Hs.129057	Hs.250822	Hs.83883	Hs.2642	Hs.250696	Hs.172928
	q23.2	q23.2	q24.2 q24.3	025.3	q25.3	p11.32	p11.32	q13.43	p11.21	p11.23	q11.1	q11.22	q13.12	q13.13	q13.2	q13.31	q13.32	q13.33	q13.1	q13.1
	17	17	71	17	: 4	2	∞ .	19	20	20	20	20	20	20	20	2	20	20	22	22
	metastatic	metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
	colon	colon	colon	r C		colon	colon	uoloo			colon	colon	colon	colon	colon	colon	colon	colon	colon	colon
	BF029215	BG165011	AI675178 U28386	A 1505000	A1323022	AF017790	AF017790	V V 7 1 0 0 2 2	22000	A1990405	AE098158	AW003586	U73379	AA207074	AF041260	AF011468	AA535819	X70940	AL035081	Y15916
	359	426	398 369		333 270	331	404	722	274	399	402	375	433	2000	430	424	435	394	367	397
	419	420	421		423 804	425	426	101	174	420	120	434	432	727	434	435	436	437	438	439

Table 1 (Continued)

hypothetical protein MGC861	ESTs	ESTs	ESTs	Homo sapiens cDNA FLJ13017 fis clone NT2RP3000628	Homo sapiens cDNA FLJ13536 fis clone PLACE1006521	PDZ domain protein (Drosophila inaD-like)	beta-amyloid binding protein precursor	ESTs	Homo sapiens cDNA FLJ12095 fis clone		p53-regulated DDA3	ESTs	apolipoprotein A-I binding protein	hypothetical protein MGC13038	cell division cycle associated 1	uridine monophosphate kinase	chromosome 1 open reading frame 19	unknown	methylene tetrahydrofolate dehydrogenase	(NAD+ dependent) methenyltetrahydrofolate	cyclonydrolase	norno sapiens similar lo Kincin conve 2510006C20 dene clone MGC:24001	IMAGE:4050858 mRNA complete cds	ribonucleotide reductase M2 polypeptide	unknown	cell division cycle associated 7	ESTs Weakly similar to hypothetical protein	FLJZ083/ [Homo sapiens] [H.sapiens]
Hs.208912	Hs.145958	Hs.120893	Hs.259438	Hs.301858	Hs.11493	Hs.321197	Hs.333541	Hs.127274	Hs.301237		Hs.77550	Hs.133294	Hs.374850	Hs.158515	Hs.234545	Hs.75939	Hs.32058	NULL	Hs.154672		400000	TS. 103223		Hs.75319	NULL	Hs.333893	Hs.144264	
q13.2	p31.3	p31.3	p31.3	p31.3	p31.3	p31.3	p32.1	p32.1	p32.1	•	q21.3	d22	q22	q22	q23.3	q23.3	q25.3	p11.1	p13.1		9	p.10.4		p25.1	q13	q31.1	p13.2	
22	<del>-</del>	<del></del>	~	_	<del></del>	<del>-</del>	~	τ-	~	•	~	~	~	~	<del></del>	<del>-</del>	~	7	~		c	7		7	7	7	2	
metastatic	primary	primary	primary	primary	primary	primary	primary	primary	primary	•	primary	primary	primary	primary	primary	primary	primary	primary	primary		•	primary		primary	primary	primary	primary	
colon	lung	lung	lung	lung	lung	lung	lung	lung	lung		gun	lung	lung	lung	lung	lung	lung	lung	lung		1	<u>gini</u>		lung	lung	lung	lung	
AI381686	AA905821	A1056599	AW070459	AK022113	AU151151	AB044807	AA012917	BF224444	AU147177		AA926959	AI053741	AI766666	AI739071	AF326731	BC002906	AA182412	AA725362	A1990317		1404001	AII8108/		AI492879	H24953	AA749314	C00851	
418	506	508	511	527	528	547	485	498	526	!	473	443	448	469	441	446	442	482	472		7	404 404		474	481	451	519	
440	441	442	443	444	445	446	447	448	449		420	451	452	453	454	455	456	457	458		( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( )	409 804		460	461	462	463	

ESTs	peptidylprolyl isomerase (cyclophilin)-like 1	high mobility group AT-hook 1	hypothetical protein FLJ30829	SRY (sex determining region Y)-box 4	hypothetical protein FLJ20958	hypothetical protein LOC51256	hypothetical protein MGC1223	epidermal growth factor receptor	(erythroblastic leukemia viral (v-erb-b)	oncogene homolog avian)	ESTS	ESTs	ESTs	ESTs	Homo sapiens clone MGC:33530	IMAGE:4820705 mRNA complete cds	LanC lantibiotic synthetase component C-like	2 (bacterial)	Homo sapiens cDNA FLJ10417 fis clone	NT2RP1000112	biliverdin reductase A	ESTs	ESTs	ESTs	ESTs Moderately similar to cytokine receptor-	like factor 2 cytokine receptor CRL2 precusor	[Homo sapiens]	histone H2A.F/Z variant	Homo sapiens cDNA: FLJ21623 fis clone	Homo sapiens mRNA cDNA DKF2p434A1014	
Hs.125249	Hs.27693	Hs.139800	Hs.201619	Hs.83484	Hs.261023	Hs.8645	Hs.273077	Hs.77432		٠	Hs.127991	Hs.252928	Hs.205559	Hs.103351	Hs.335933		Hs.134342		Hs.180171		Hs.81029	Hs.284148	Hs.296098	Hs.152895	Hs.222015			Hs.301005	Hs.306791	Hs.332520	
p15.1	p21.2	p21.31	p22.3	p22.3	p23	p24.1	p24.2	p11.2			p11.2	p11.2	p11.2	p11.2	p11.2		p11.2		p12.3		p13	p13	p13	p13	p13			p13	p13	p13	-
S	ဖ	ဖ	ဖ	9	ဖ	ဖ	9	7			7	/	7	7	7		7		7		7	_	_	7	7		I	_	_	7	
primary	primary	primary	primary	primary	primary	primary	primary	primary			primary	primary	primary	primary	primary		primary		primary		primary	primary	primary	primary	primary		•	primary	primary	primary	•
lung	lung	gun	lung	lung	lung	lung	lung	lung			lung	nug	lung	lung	lung		lung		lung		Jung	lung	lung	lung	lung			gunj .	gunj	lung	)
AA383208	AA524353	AW005489	AI677701	BG528420	Al439141	AI279547	W27692	K03193			A1806160	AW138673	H65306	AW971863	D60436		AI363001		AV700815		AA740186	AI252004	AW452419	AI418313	AI191118			AI823792	AK025276	AL137266	
458	548	522	538	551	467	539	540	495			496	497	205	203	536		545		524		486	510	514	515	517		Č	523	533	534	
464	465	466	467	468	469	470	471	472			473	474	475	476	477		478		479		480	481	482	483	484		į	480 60 60	486	487	

Table 1 (Continued)

		<u>-(</u>						~		ge									970	5										
(from clone DKFZp434A1014) partial cds	hypothetical protein MGC4607	NPC1 (Niemann-Pick disease type C1 gene)- like 1	serine/threonine kinase 17a (apoptosis-inducina)	hynothetical protein MGC2824	ICE-II mony binding profess 3	For the first Arbitral protein 5	Hypothetical protein DC0 (233)	membrane protein palmitoylated 6 (MAGUK	p55 subfamily member 6)	DNA directed RNA polymerase II polypeptide	J-related gene	scribble	carbonic anhydrase VIII	ESTS	ESTS	pituitary tumor-transforming 1	unknown	unknown	Homo saniens mRNA CONA DKEZn566A1046	(from clone DKFZn566A1046)	ESTS	ESTs	Homo sapiens cDNA FLJ14180 fis clone	NT2RP2003799	Homo sapiens cDNA FLJ34367 fis clone FEBRA2016621	tumor protein D52	ESTS	cadherin 17 Ll cadherin (liver-intestine)	cyclin E2	
	Hs.9960	Hs.47701	Hs.9075	Hs. 59594	He 70440	113.7.3440 Ho 97395	19.07.00	HS.108931		Hs.375569		Hs.239784	Hs.250502	Hs.12664	Hs.19107	Hs.252587	NOF	JIN.	Hs 168950		Hs.133293	Hs.128841	Hs.296753		Hs.60681	Hs.2384	Hs.184387	Hs.89436	Hs.30464	
	p13	p13	p13	D14.1	7.7.7.3	ב ה ה ה	7 / 5 r	p15.3		q22.1		NOLL	q12.2	a13.2	a13.2	q13.2	α13.3	a13.3	021.11	: !	q21.11	q21.11	q21.11		q21.11	q21.13	q21.13	q22.1	q22.1	
	7	7	7	7	^	- 1-	- 1	•	1	7		ω	ω	ω	∞	ω	œ	∞	ω	)	ω	∞	ω		œ	ω	ω	ω	∞	
	primary	primary	primary	primary	primary	primary	, mind	primary		primary		primary	primary	primary	primary	primary	primary	primary	primary		primary	primary	primary		primary	primary	primary	primary	primary	
	lung	lung	lung	luna	בו בו	9 L	D 1	Buni	•	gun		lung	lung	lung	lung	lung	lung	lung	luna		lung	lung	gunj	,	lung	gunj	lung	lung	lung	
	BC004903	AF192523	AW194730	BC000769	U97188	A1910524	VIOVE 400	A1000405		AW402635		AI922792	R51273	BE465243	AA132172	AA203476	AF232217	AF130055	BF002104		AI335223	AI370381	AK024242		AI701468	BG389015	AA479492	U07969	AF091433	
	542	546	550	541	445	465	17.	<b>1</b>	į	494		475	489	200	503	549	555	556	463		202	512	529	6	230	480	499	488	491	
	488	489	490	491	492	493	707	† 0 †	L	495		496	497	498	499	200	501	502	503		504	505	206	1	20.7	208	209	510	511	

Table 1 (Continued)

collagen triple helix repeat containing 1	ESTs	hypothetical protein MGC5254	development and differentiation enhancing factor 1	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens] KIAA1485 profein	Homo saniens mRNA cDNA DKFZp451M139	(from clone DKFZp451M139)	hypothetical protein FLJ11088	DKFZP564O1863 protein	hypothetical protein FLJ10637	KIAA1340 protein	serine/threonine kinase 38 like	SRB7 suppressor of RNA polymerase B	homolog (yeast)	unknown	ESTs	Homo sapiens cDNA FLJ11335 fis clone	PLACE1010630	Homo sapiens cDNA FLJ34764 fis clone NT2NE2002311	transcription factor BMAL2	branched chain aminotransferase 1 cytosolic	Homo sapiens cDNA FLJ13318 fis clone OVARC1001600	Homo sapiens cDNA: FLJ21962 fis clone HEP05564	Homo sapiens mRNA cDNA DKFZp564F2072 (from clone DKFZp564F2072)	hypothetical protein MGC10946	
Hs.283713	Hs.130107	Hs.222088	Hs.10669	Hs.20247	Uc 15611	Hs 176669		Hs.227591	Hs.173074	Hs.22595	Hs.51743	Hs.184523	Hs.286145		NOLL	Hs.221024	Hs.284270		Hs.111583	Hs.222024	Hs.317432	Hs.296734	Hs.7567	Hs.301210	Hs.170994	
q22.3	q22.3	q24.13	q24.22	q24.22	70 70	424.62	44.60	p11.22	p11.23	p11.23	p11.23	p11.23	p11.23		p11.23	p11.23	p11.23		p11.23	p11.23	p12.1	p12.1	p12.1	p12.1	p12.1	
ω	ω	ω	ω	∞	o	οα	<b>o</b>	12	12	12	12	12	42		12	12	12		12	7	12	12	12	12	12	
primary	primary	primary	primary	primary		primary primary	pillial g	primary	primary	primary	primary	primary	primary	:	primary	primary	primary		primary	primary	primary	primary	primary	primary	primary	
lung	lung	lung	lung	lung	!	gun!	D D	Jung	lung	lung	lung	lund	lung	•	lung	lung	lung		lung	lung	nng In	gun]	lung	lung	lung	
AA584310	AA904882	AA451665	W03103	BF055351		BF941325	AWISTURS	AA447947	R91766	AF274950	AI334297	AW779556	AI688580		AF161472	BF724206	AL118653		AI652982	AA127950	AI652662	AU154905	AK025615	AA829940	BE326710	
490	505	543	493	518		544	222	537	456	466	470	476	478		483	504	525		531	553	449	460	461	462	468	
512	513	514	515	516	į	517	218	519	520	521	522	523	524		525	526	527		528	529	530	531	532	533	534	

															•															
	homolog ESTs		ethanolamine kinase		domains 1	H2A histone family member J	C2f protein		polypeptide 11 (CHL1-like helicase homolog S.	cerevisiae)	forkhead box M1	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	androgen-regulated short-chain	dehydrogenase/reductase 1	ESTs	Homo sapiens cDNA FLJ36057 fis clone	TESTI2018475 highly similar to 1 AMININ	ALPHA-1 CHAIN PRECURSOR	highly expressed in cancer rich in leucine	heptad repeats	BTB (POZ) domain containing 3	ESTs	Synaptosomal-associated profein 25kDa	chromograpin B (secretograpin 1)	chromosome 20 open reading frame 130	chromosome 20 open reading frame 07	solute cerrier family 4 sodium biochemos	transportor life member 44	transcription factor AP-2 gamma (activating
Hs.351221	Hs.58086	Hs.137003	Hs.120439	Hs.108106		Hs.36727	Hs.12045	Hs.380623			Hs.239	Hs.84113		Hs.179817		Hs.373550	Hs.48659			Hs.58169		Hs.7935	Hs.70903	Hs.84389	Hs.2281	Hs.135056	Hs 26802	Hs. 105607		Hs.61796
p12.1	p12.1	p12.1	p12.1	p12.2		p12.3	p13.31	p13.31			p13.33	q22.1		q23.2		p11.31	p11.31			p11.32	•	p12.2	p12.2	p12.2	p12.3	513	p.13	p13	-	q13.31
12	12	12	12	12		12	12	12			12	4		4		<u>დ</u>	18			<u>დ</u>		20	20	20	20	20	20	20		20
primary	primary	primary	primary	primary		primary	primary	primary			primary	primary		primary		primary	primary			primary	•	primary	primary	primary	primary	primary	primary	primary	•	primary
lung	lung	gun	gun	lung		gun.	gun	lung			gun.	lung		lung		gun!	mg			lung	1	gun.	gun.	lung	gunj	lung	lung	lung	)	lung
AA015609	W70242	AI242023	A1003792	AA669106		BC003602	AI392836	AI983033		174640	0/4612	AF213033	7	AF16/438		AI146765	AW003207			AF01//90	0010000	ADUZ2 109	AI/32446	U21267	Y00064	A1096882	AI949781	AI924533		U85658
484	501	576 200	520	554		459 109	48/	492		100	170	455	,	44/		513 505	225			4 4 4 4	750	ָ ֭֭֓֞֝֞֝֞֝֞֝֓֓֓֓֝֡֓֡֓֓֓֓֡֓֡֓֓֡֓֡֓֡֓֡֓֡֓֡֓֡֓֡֡֡֡֡֡֓֡֓֡֓֡֓֡	45/	4/9	452	453	454	477		552
535	536	737	238 200	950	0.4	04C	541	542		573	2:	244	27	040	074	040 140	247		6	240	5/10	) L	000		225	553	554	555		556

enhancer binding protein 2 gamma)	heparan sulfate 2-O-sulfotransferase 1	ESTs Moderately similar to hypothetical	protein FLJ20378 [Homo sapiens] [H.sapiens]	hypothetical protein FLJ20354	G-protein gamma-12 subunit	PAI-1 mRNA-binding protein	Homo sapiens cDNA: FLJ23597 fis clone	ENG 1920 I Fas (TNFRSE6) associated factor 1	DKF7P77A071 protein	unknown	p53-requiated DDA3	apolipoprotein A-I binding protein	ESTS	hypothetical protein MGC13038	cell division cycle associated 1	uridine monophosphate kinase	chromosome 1 open reading frame 19	unknown	methylene tetrahydrofolate dehydrogenase	(NAD+ dependent) methenyltetrahydrofolate	cyclohydrolase	Homo sapiens Similar to RIKEN cDNA	2510006C20 gene clone MGC:24001	IMAGE:4050858 mRNA complete cds	ribonucleotide reductase M2 polypeptide	unknown	cell division cycle associated 7	ESTs	hypothetical protein FLJ20958
	Hs. 169939	Hs.374411		Hs.133260	Hs.8107	Hs.165998	Hs.299254	Hs 25821	Hs.13036	NULL	Hs.77550	Hs.374850	Hs.133294	Hs.158515	Hs.234545	Hs.75939	Hs.32058	NOLL	Hs.154672			Hs.105223			Hs.75319	NOLL	Hs.333893	Hs.125249	Hs.261023
	p22.3	p31.1		p31.2	p31.2	p31.2	p32.1	p32.3	p32.3	p34.1	q21.3	q22	q22	d22	q23.3	q23.3	q25.3	p11.1	p13.1			p16.2			p25.1	q13	a31.1	p15.1	p23
	~	~		<del></del>	~	Ψ-	~	<del>-</del>	<del>-</del>	~	<del>-</del>	~	<del>-</del>	_	_	<del>-</del>	<del>-</del>	7	7			~			7	7	7	5	9
•	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic			metastatic			metastatic	metastatic	metastatic	metastatic	metastatic
. •	lung	lung		lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung	lung			gun			lung	lung	lung	lung	gun
	AW151887	BE645144		AI810054	N32508	BC002488	AA618420	AW140098	AW409848	AF151063	AA926959	AI766666	AI690773	AI739071	AF326731	D78335	AA182412	AA725362	AI990317			AI19189/			BC001886	H24953	AA749314	AA868748	Al439141
	654	651		619	629	636	628	627	648	637	000	576	588	601	561	262	558	299	292			603			583	605	575	579	289
	222	258	1	559	260	261	262	563	564	565	266	267	268	269 2	270	571	572	573	574		1	c/c		1	9/0	277	278	579	280

Table 1 (Continued)

Homo sapiens cDNA FLJ13503 fis clone	PLACE1004838 unknown	Homo sapiens cDNA FLJ25559 fis clone JTH02834	Homo sapiens cDNA FLJ20099 fis clone COL04544	Homo sapiens cDNA FLJ12308 fis clone MAMMA1001931	chaperonin containing TCP1 subunit 6A (zeta	epidermal growth factor receptor	(erythroblastic leukemia viral (v-erb-b)	Homo sapiens cDNA: FLJ23165 fis clone LNG09846	anillin actin binding protein (scraps homolog	Drosophila)	IGF-II mRNA-binding protein 3	hypothetical protein BC012331	membrane protein palmitoylated 6 (MAGUK	p55 subfamily member 6)	claudin 12	Homo sapiens cDNA: FLJ23160 fis clone LNG09682	unknown	met proto-oncogene (hepatocyte growth factor	putative methyltransferase	Secretory profein SEC8	scribble	cDNA for differentially expressed CO16 gene
Hs.287577	NOLL	Hs.140489	Hs.272227	Hs.188082	Hs.82916	Hs.77432		Hs.279898	Hs.62180	:	Hs.79440	Hs.87385	Hs.108931		Hs.258576	Hs.118258	NOLL	Hs.285754	Hs.233694	Hs.107394	Hs.239784	Hs.69517
p11.2	p11.2	p11.2	p11.2	p11.2	p11.2	p11.2		p11.2	p14.2		p15.3	p15.3	p15.3		q21.13	q21.13	q31.2	q31.2	q32.1	d33	NULL	NOLL
7	7	~	7	_	7	7		_	7	1	_	~	7	i	/	7	7	7	7	7	ω	ω
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic	metastatic	:	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic
lung	lung	lung	lung	lung	lung	lung		lung	lung	1	Bun.	gun	lung	_	gun.	lung	lung	lung	lung	lung	lung	lung
AU156822	U48722	AA768884	AK000106 ·	AU147861	BE737030	AW157070		BE878463	AK023208	007700	097.188	AI910524	AI806483	700110	AL136//0	B-680588	U19348	BG170541	AI632244	AI964022	AI922792	AA723810
909	209	609	610	613	616	622		639	222	200	200	//6	280	7	/[0	035 035	618	638	641	653	593	644
581	582	583	584	585	586	287		288	289	200	0 0	28.1	285	60	0 0 0 0	0 1 0 (4	595	296	282	298	299	009

ESTs	ESTs	aspartate beta-hydroxylase	ring finger protein 29	Homo sapiens mRNA cDNA DKFZp566A1046	(from clone DKFZp566A1046)	Homo sapiens cDNA: FLJ21569 fis clone	COL06508	hypothetical protein FLJ11011	ESTs Weakly similar to retinal short-chain	dehydrogenase/reductase retSDR2 [Homo	sapiens] [H.sapiens]	transcription elongation factor B (SIII)	polypeptide 1 (15kDa elongin C)	staufen RNA binding protein homolog 2	(Drosophila)	tumor protein D52	hypothetical protein MGC22825	zinc finger protein RINZF	Homo sapiens cDNA FLJ23705 fis clone	HEP11066	calcitonin/calcitonin-related polypeptide alpha	transcription factor BMAL2	hypothetical protein FLJ10637	unknown	SRB7 suppressor of RNA polymerase B	homolog (yeast)	DKFZP564O1863 protein	KIAA1340 protein	serine/threonine kinase 38 like	Homo sapiens cDNA FLJ34764 fis clone	NT2NE2002311
Hs.29419	Hs.152409	Hs.283664	Hs.85524	Hs.168950		Hs.121194		Hs.21275	Hs.356086			Hs.184693		Hs.96870		Hs.2384	Hs.183861	Hs.237146	Hs.49136		Hs.37058	Hs.222024	Hs.22595	NOLL	Hs.286145		Hs.173074	Hs.51743	Hs.184523	Hs.111583	
q12.3	q12.3	q12.3	q13.1	q21.11		q21.11		q21.11	q21.11			q21.11		q21.11		q21.13	q21.13	q21.13	q24.21	•	p15.2	p11.23	p11.23	p11.23	p11.23		p11.23	p11.23	p11.23	p11.23	
ω	∞	ω	ω	œ		∞		∞	ω			ω		ω		∞	ω	ω	ω		7	12	12	7	12		2	12	12	12	
metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic			metastatic		metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	
lung	gun	lung	gun	lung		lung		lung	lung			gunj		lung		<u>gun</u>	lung	lung	lung		lung	lung	lung	lung	lung		lung	lung	lung	lung	
BF059124	AA543030	AF289489	AW663544	BF002104		AI916600	)	AI625741	AW150720			N89607		W46994		BG389015	AK000049	AK024296	AL039862		M26095	AF256215	AI569851	AF161472	U46837		R91766	AI334297	AW779556	BF540749	
621	631	632	646	581		612		623	030 030		!	645		650	•	563	633	634	656		611	565	566	573	574		280	584	585	586	
601	602	· 603	604	605		909		209	809		,	609		610		611	612	613	614		615	616	617	618	619		620	621	622	623	

Table 1 (Continued)

seven transmembrane protein TM7SF3 branched chain aminotransferase 1 cytosolic Homo sapiens cDNA: FLJ21962 fis clone	HEPUSS64 hypothetical protein MGC10946 Homo sapiens mRNA cDNA DKFZp564F2072	(from clone DKFZp564F2072) v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene	homolog Homo sapiens cDNA FLJ13318 fis clone	ubiquitin-like containing PHD and RING finger	domains 1 H2A histone family member J	Homo sapiens cDNA FLJ36082 fis clone TESTI2019998	bromodomain adjacent to zinc finger domain	ESTS	ERO1-like (S. cerevisiae)	hypothetical protein FLJ12618	WW45 protein	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	glia maturation factor beta	glutatnione peroxidase 2 (gastrointestinal)	ESIS	androgen-regulated short-chain	dehydrogenase/reductase 1 Homo sapiens cDNA FLJ37574 fis clone	BRCOC2003100 hypothetical protein FLJ39091
Hs.10071 Hs.317432 Hs.7567	Hs.170994 Hs.301210	Hs.351221	Hs.296734	Hs.108106	Hs.36727	US.3220/9	Hs.8858	Hs.146134	Hs.25740	Hs.222021	Hs.288906	Hs.84113		HS.151413	IS.Z/04	HS.9/849	Hs.179817	Hs.43397	Hs.98365
p11.23 p12.1 p12.1	p12.1 p12.1	p12.1	p12.1	p12.2	p12.3	- - -	q12	q13.1	q21.3	q21.3	q21.3	q22.1	0	922.1	420. I	923.1	q23.2	q23.2	q24.2
444	12 2	12	12	7	5 5	7	4	4	4	4	4	4	7	<u> </u>	t <u> </u>	4	<del>7</del>	4	4
metastatic metastatic metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	וויפומאומווי	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	.;,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	metastatic	motostatic	metastatic	metastatic	metastatic	metastatic
lung lung lung	lung lung	lung	lung	lung	lung	20 .	lung	lung	lung	gun	gun	lung	-	ביין ביין	בי בי בי	Din.	lung	lung	lung
BC005176 Al652662 AK025615	BE326710 AA829940	AA015609	AU154905	AK025578	BC003602		AA102574	A1953589	AW268365	BC006117	AJ292969	AF213033	BCOOKSEO	A1985034	A1554514	+10+000	AF167438	AI654093	BE465894
587 564 568	570 595	597	604	571	578	2 6	642	620	809	626	655	26/	652	614	624	1 000	569	625	647
624 625 626	627 628	629	630	631	632		634	635	636	637	638 638	639	640	641	642	1 6	643	644	645

Table 1 (Continued)

chromogranin A (parathyroid secretory protein 1)	hypothetical protein FLJ21916 Homo sapiens cDNA FLJ40513 fis clone	highly expressed in cancer rich in leucine heptad repeats	synaptosomal-associated protein 25kDa	ESIS DTB (DA3) domain containing 3	BTB (POZ) domain containing 5 chromograpia B (secretograpia 1)	chromosome 20 open reading frame 97	solute carrier family 4 sodium bicarbonate	transporter-like member 11	chromosome 20 open reading frame 139	hypothetical protein FLJ20354	ESTs	ESTs	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	HSPC150 protein similar to ubiquitin-	conjugating enzyme	centromere protein F 350/400ka (mitosin)	ribonucleotide reductase M2 polypeptide	hairy and enhancer of split 6 (Drosophila)	cyclin B1	paired-like homeodomain transcription factor 1	hypothetical protein BC003515	Homo sapiens cDNA FLJ11041 fis clone		inhibin beta A (activin A activin AB alpha
Hs.172216	Hs.90034 Hs.374662	Hs.58169	Hs.84389	Hs.70903	HS./933 Hs 2281	Hs.26802	Hs.105607		Hs.135056	Hs.133260	Hs. 133294	Hs.133294	Hs.127310	ı	Hs.234545	Hs.5199		Hs.77204	Hs.75319	Hs.42949	Hs.23960	Hs.84136	Hs.284207	Hs.28792		Hs.727
q32.11	q32.11 q32.12	p11.32	p12.2	p12.2	p12.2	p.12.0	p13		p13	p31.2	d22	q22	q23.2		q23.3	q32.1		q32.3	p25.1	q37.3	q13.2	q31.1	p21.2	p14.1		p14.1
4	<del>4</del> <del>4</del>	18	20	200	2 6	202	20		20		~	<del>-</del>	~		<del></del>	<del>-</del>		_	7	7	2	2	ဖ	7	i	^
metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	primary	primary	primary	primary		primary	primary		primary					primary			primary
lung	lung lung	lung	lung	gun]	gun!	בים בים בים	gun	•	lung	prostate	prostate	prostate	prostate		prostate	prostate	•	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate
AI969102	AI656232 AI670847	AF017790	D21267	AI732446	AB023169	A1949781	AF336127		A1096882	AK000490	AW271106	AI053741	AA830844		AF326731	AB032931		U30872	AI492879	N21131	BE407516	U70370	BE794699	AI343467		M13436
615	640 649	559	591	598	602	7 22	594		596	662	629	099	663		657	661		658	684	683	069	691	692	694		695
646	647 648	649	650	651	652	000 654	655		656	657	658	629	099		661	662		663	664	665	999	299	899	699		029

Table 1 (Continued)

polypeptide) anillin actin binding protein (scraps homolog Drosophila)	T-LAK cell-originated protein kinase	pituitary tumor-transforming 1	hypothetical protein MGC5254	Homo sapiens Similar to RIKEN cDNA	3321402G02 gene clone MGC:23929 IMAGE:4807540 mRNA complete cds	ESTs Weakly similar to T2D3_HUMAN	Transcription initiation factor TFIID 135 kDa subunit (TAFII-135) (TAFII135)	cell division cycle 2 G1 to S and G2 to M	hypothetical protein FLJ10540	similar to RIKEN cDNA 2610036L13	forkhead box M1	Human clone 295 5cM region surrounding	hepatocyte nuclear factor-1a/MODY3 mRNA	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	MAD2 mitotic arrest deficient-like 1 (yeast)	cyclin B2	KIAA0101 gene product	solute carrier family 7 (cationic amino acid	transporter y+ system) member 5	hypothetical protein MGC4692	hypothetical protein BC014072	mitotic spindle coiled-coil related protein	ESTs Moderately similar to TP2A_HUMAN	DNA topoisomerase II alpha isozyme	[H.sapiens]	topoisomerase (DINA) II alpha 170kDa
Hs.62180	Hs.104741	Hs.252587	Hs.222088	Hs.352417		Hs.323445		Hs.334562	Hs.14559	Hs.23044	Hs.239	Hs.204166		Hs.84113		Hs.79078	Hs.194698	Hs.81892	Hs.184601		Hs.13561	Hs.348504	Hs.16244	Hs.370428		7	Hs.156346
p14.2	p21.1	q13.2	q24.13	q33.2		q34.3	•	q21.2	q23.33	q13.1	p13.33	q24.31		q22.1		q23.1	q21.3	q22.2	NOLL		p13.3	q11.2	q11.2	q21.31	•	3	q21.31
7	ω (	∞ (	∞	ဝ		တ		9	9	7	12	12		4		4	15	15	16		16	17	17	17		į	17
primary	primary	primary	primary	primary		primary		primary	primary	primary	primary	primary		primary	•	primary	primary	primary	primary		primary	primary	primary	primary		•	primary
prostate	prostate	prostate	prostate	prostate	_	prostate	_	prostate	prostate	prostate	prostate	prostate	_	prostate	_	prostate	prostate	prostate	prostate	_	prostate	prostate	prostate	prostate		•	prostate
AK023208	A1932328	AA203476	A1925583	BE544837		A1983261		X05360	AI674163	BE614410	U74612	R61322		L25876		<b>U65410</b>	AL080146	D14657	AB018009		AI819340	BE328850	AF063308	AW003286			AI375913
693	869	269	969	200		669		664	665	999	299	899		699		670	671	672	674		673	678	629	929	) •		089
671	672	673	674	675		929	)	677	678	629	680	681		682		683	684	685	989		687	688	689	069	) )		691

unknown ESTs Weakly similar to hypothetical protein	r LJZบ4ชษ [Homo sapiens] [H.sapiens] ESTs	ubiquitin UBF-fl	KIAA0186 gene product	chromosome 20 open reading frame 1	ubiquitin-conjugating enzyme E2C	serine/threonine kinase 6	holocarboxylase synthetase (biotin-[proprionyl- Coenzyme A-carboxylase (ATD-byydrolyging)1	igase)	hypothetical protein MGC861	proteasome (prosome macropain) subunit beta	type 4	ESTs	ESTs	apolipoprotein A-I binding protein	kinase interacting with leukemia-associated	gene (stathmin)	cell division cycle associated 1	hypothetical protein MGC17528	hypothetical gene supported by BC007071	centromere protein F 350/400ka (mitosin)	chorionic somatomammotropin hormone 2	hypothetical protein FLJ22969	endothelial and smooth muscle cell-derived	neuropilin-like protein	SMC4 structural maintenance of	chromosomes 4-like 1 (yeast)	SMC4 structural maintenance of	chromosomes 4-like 1 (yeast)
NULL u Hs.165909 E		_	Hs.36232 K	Hs.9329 c	Hs.93002 u	Hs.250822 s	Hs.79375 h	) <u>.</u>	Hs.208912 h	Hs.89545 p	<b>t</b>	Hs.133294 E	Hs.133294 E	Hs.374850 a	Hs.127310 ki		Hs.234545 co	Hs.300893 h	Hs.117305 h	Hs.77204 ce	Hs.334372 cl		Hs.173374 el	č	Hs.50758 S		Hs.50758 SI	ਹ
q21.31 q23.2	q23.3	q13.43	p11.21	q11.1	q13.12	q13.31	q22.13		q13.2	q21.2		<b>q</b> 22	<b>4</b> 22	d22	q23.2		q23.3	q24.3	q31.1	q32.3	q42.2	p21.32	q12.3		q26.1		q26.1	
17	17	9	20	20	20	70	21		22	<del>-</del>		τ-	_	<del>-</del>	<del>-</del>		τ-	<del>-</del>	τ	<del>-</del>	<del></del>	က	က		က	•	က	
primary primary	primary	primary	-primary	primary	primary	primary	primary		primary	metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	٠.	metastatic		metastatic	
prostate prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate	prostate		prostate	prostate	prostate	prostate		prostate	prostate	prostate	prostate	prostate	prostate	prostate	:	prostate	1	prostate	
L47276 BG165011	BF056791	AA/19022	D80008	AF098158	U73379	AF011468	T77624		AI381686	AA630330		AW271106	AI690773	AI766666	AI249980		AI015982	H62656	N29457	U30872	AA151971	AI971357	W24316		AI338462	700000	AB01998/	
681 677	675	789	989	685	688	687	701	. (	689	723		771	773	803	739	0	86/	745	753	96/	794	748	778		716	7,47	/1./	٠
692 693	694	င္ပန္ပဝ	969	269	869	669	200		701	702	ļ	703	704	705	902	1	/0/	708	607	710	711	712	713	,	714	7.7	CI./	÷

Table 1 (Continued)

KIAA1363 protein epithelial cell transforming sequence 2	oncogene unknown proteasome (prosome macropain) 26S subunit	non-ATPase 2 heat shock 60kDa protein 1 (chaperonin) unknown	thyroid hormone receptor interactor 13 cyclin B1 Homo sapiens cDNA FLJ11842 fis clone	HEMBA1006652 weakly similar to 60S RIBOSOMAL PROTEIN L7 anillin actin binding protein (scraps homolog	Drosophila) hypothetical protein BC012331 replication protein A3 14kDa	paternally expressed 10 ESTs Highly similar to asparagine synthetase	[Homo sapiens] [H.sapiens] polymerase (RNA) II (DNA directed)	polypeptide J 13.3kDa met proto-oncogene (hepatocyte growth factor	receptor) ESTs Weakly similar to hypothetical protein	PLJ20378 [Homo sapiens] [H.sapiens] exosome component Rrp41 nucleophosmin (nucleolar phosphoprotein B23	numatrin) aspartate beta-hydroxylase pituitary tumor-transforming 1 CGI-83 protein
Hs.22941 Hs.122579	NULL Hs.74619	Hs.79037 NULL	Hs.6566 Hs.23960 Hs.374582	Hs.62180	Hs.87385 Hs.1608	Hs.137476 Hs.370106	Hs.80475	Hs.285754	Hs.369347	Hs.343589 Hs.9614	Hs.283664 Hs.252587 Hs.118554
q26.32 q26.32	q26.33 q28	p14.3 p15.1	p15.33 q13.2 p21.1	p14.2	p15.3 p21.3	q21.3 q21.3	q22.1	q31.2	433	NULL q12.1	q12.3 q13.2 q13.3
ოო	ოო	ည	യ വ	7	~ ~	~ ~	7	_	7	<b>ω</b> ω	ထထထ
metastatic metastatic	metastatic metastatic	metastatic metastatic	metastatic metastatic metastatic	metastatic	metastatic metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic metastatic	metastatic metastatic metastatic
prostate prostate	prostate prostate	prostate prostate	prostate prostate prostate	prostate	prostate prostate	prostate prostate	prostate	prostate	prostate	prostate prostate	prostate prostate prostate
AL119157 BG170335	AI968388 AA194529	BE256479 AI750154	U96131 M25753 Al369840	AK023208	AI910524 L07493	AL582836 Al922470	L37127	AA193396	AI679933	AI571298 AA191576	AW001796 AA203476 AI525903
740	704 724	760 705	787 758 758	804	752 721	770	726	736	768	763 732	801 729 795
716 717	718 719	720	723	725	726	729	730	731	732	733 734	735 736 737

	polypeptide i (TokDa elongin C) DKFZP56400463 protein	collagen triple helix repeat containing 1	ESTs Moderately similar to leucine-rich	neuronal protein [Homo sapiens] [H.sapiens]	chronic myelogenous leukemia tumor antigen	99	mal T-cell differentiation protein 2	Homo sapiens mRNA cDNA DKFZp666E036	(from clone DKFZp666E036)	development and differentiation enhancing	factor 1	unknown	ZW10 interactor	cell division cycle 2 G1 to S and G2 to M	apoptosis-inducing factor (AIF)-homologous	mitochondrion-associated inducer of death	plasminogen activator urokinase	adenosine kinase	potassium large conductance calcium-	activated channel subfamily M alpha member		M-phase phosphoprotein 1	hypothetical protein FLJ10540	similar to RIKEN cDNA 2610036L13	FOS-like antigen 1	myeloma overexpressed gene (in a subset of	t(11 14) positive multiple myelomas)	Rac GTPase activating protein 1	hypothetical protein from clone 643	Homo sapiens clone MGC:20874
Hs.184693	Hs.273344	Hs.283713	Hs.127286		Hs.195870		Hs.76550	Hs.356036		Hs.10669		NULL	Hs.42650	Hs.334562	Hs.117062		Hs.77274	Hs.94382	Hs.89463			Hs.240	Hs.14559	Hs.23044	Hs.283565	Hs.116051		Hs.23900	Hs.206501	Hs.121973
q21.11	q22.3	q22.3	q23.1		q23.2		q24.12	q24.22		q24.22		q24.23	q21.1	q21.2	q22.1		q22.2	q22.2	q22.3			q23.31	q23.33	q13.1	a13.1	q13.3		q13.12	q13.12	q13.12
∞	œ	∞	ω		ω		ω	∞		∞		∞	9	9	9		9	9	9			9	9	Ţ	=	7		12	75	12
metastatic	metastatic	metastatic	metastatic		metastatic		metastatic	metastatic		metastatic		metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic			metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic
prostate	prostate	prostate	prostate		prostate		prostate	prostate		prostate		prostate	prostate	prostate	prostate		prostate	prostate	prostate			prostate	prostate	prostate	prostate	prostate		prostate	prostate	prostate
AA995715	BE409290	AA584310	BF109660		AI802955		AL117612	AI880004		AI023398	<b>-</b>	AA527374	AF067656	AF154332	BC006121		K03226	U90339	AI198535		071	NZ/428	AI674163	BE614410	BG251266	AA621983		U82984	AF091087	A1936946
710	782	788	769	i	789		737	756		784		206	702	799	802		728	802	725		1	734	751	718	.761	733	i	722	/4/	104
738	739	740	741	(	742	!	743	744		745		746	747	748	749	· (	750	751	752		1	2 2 1	154	755	756	757	1	758	709	00/

IMAGE:4547239 mRNA complete cds	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-	acetylgalactosaminyltransterase 6 (GalNAc- T6)	keratin hair basic 1	extra spindle poles like 1 (S. cerevisiae)	polymerase (DNA directed) epsilon 2 (p59	subunit)	hypothetical protein MGC20689	hypothetical protein FLJ12618	hypothetical protein FLJ10607 similar to	glucosamine-phosphate N-acetyltransferase	ERO1-like (S. cerevisiae)	Drosophila discs large-1 tumor sunressor-like	cyclin-dependent kinase inhibitor 3 (CDK2-	associated dual specificity phosphatase)	ESTs Weakly similar to PSA3 HUMAN	Proteasome subunit alpha type 3 (Proteasome	component C8) (Macropain	methylenetetrahydrofolate dehydrogenase	(NADP+ dependent) methenyltetrahydrofolate	cyclohydrolase formyltetrahydrofolate	Syllinetase	MAD2 mitotic arrest deficient-like 1 (yeast)	p53-regulated DDA3	eukarvotic franslation initiation factor s	dynein cytonlasmic heavy nohypertide 4	Cyclin-denendent kingse 2 interacting material	CDC/2 binding motion limited actual protein	CDC42 billiding protein kinase beta (UMPK- like)	hypothetical protein MGC13251
	Hs.151678		Hs.32952	Hs.153479	Hs.99185		Hs.374811	Hs.222021	Hs.27931		Hs.25740	Hs.77695	Hs.84113		Hs.301231			Hs.172665			1	HS./90/8	Hs.77550	Hs.334810	Hs.7720	Hs 38205	He 12908	13.12300	Hs.317821
	q13.13		q13.13	q13.13	q21.2		q21.2	q21.3	q21.3		q21.3	q22.1	q22.1		q22.2			q23.1			7 00	943.1	q32.12	q32.2	q32.2	a32.2	432.2	401.1	q32.31
	12		12	12	4	,	7	4	4		7	4	14		4		,	4			7	<del>-</del> ;	14	4	4	7	14	-	4
	metastatic		metastatic	metastatic	metastatic	;	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	;	metastatic			metastatic			motostio	Helasialic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic
	prostate		prostate	prostate	prostate	•	prostate	prostate	prostate	•	prostate	prostate	prostate		prostate			prostate			nroctata	prostate	prostate	prostate	prostate	prostate	prostate		prostate
	AL118633		X81420	079987	AF025840	000000	AA648933	BC006117	AI924/94	100001414	AW268365	D13633	L25876	777007	A141/084		10000	10400			1165410	A A D S O E O	AA920939	AL080102	BF000332	AI525727	AI761729		T65554
1	/0/		747	79/	727	777	144	749	06/	1	100	08/ 18/	(82	766	00/		725				738	724	5 6	/64	6//	786	800		746
7	<b>1</b> 9/		762	3 6	/64	705	766	100	/0/	760	100	100	2	77.4			772	7//			773	77.4	1 1 1	0	9//	111	778		779

Homo sapiens clone MGC:16771 IMAGE:3907551 mRNA complete cds	cell division cycle associated 4 solute carrier family 16 (monocarboxylic acid transporters) member 3	transponers) ineriner 3 ESTs	hypothetical protein PRO1855	ESTs	ESTs Weakly similar to hypothetical protein	FLJ20489 [Homo sapiens] [H.sapiens] karyopherin alpha 2 (RAG cohort 1 importin	alpna 1) thvmidine kinase 1 soluble	signal recognition particle 68kDa	hematological and neurological expressed 1	ESTs	discs large (Drosophila) homolog-associated	protein 1	thymidylate synthetase	ubiquitin carrier protein	ubiquitin UBF-fl	chromosome 20 open reading frame 27	chromosome 20 open reading frame 139	serine/threonine kinase 6	solute carrier family 21 (organic anion	transporter) member 12	eukaryotic translation elongation factor 1 alpha	chromosome 21 open reading frame 45	WD repeat domain 4	Homo sapiens cDNA FLJ35467 fis clone SMINT2005624
Hs.72363	Hs.34045 Hs.85838	Hs.201390	Hs.283558	Hs.298564	Hs.165909	Hs.159557	Hs. 105097	Hs.273307	Hs.109706	Hs.127716	Hs.75814		Hs.82962	Hs.174070	Hs.288549	Hs.274422	Hs.135056	Hs.250822	Hs.235782		Hs.2642	Hs.49932	Hs.143638	Hs.282961
q32.31	q32.31 NULL	NULL	q22	q22	q23.2	q24.3	g25.3	q25.3	q25.3	p11.22	p11.31		p11.32	q13.42	q13.43	p13	p13	q13.31	q13.33		q13.33	q22.11	q22.3	q22.3
4	47	17	17	17	17	17	17	17	17	9	48		9	19	19	20	20	20	20		70	21	21	77
metastatic	metastatic metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic	metastatic	metastatic
prostate	prostate prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate	prostate	prostate	prostate	prostate	prostate	prostate	•	prostate	prostate	prostate	prostate
H04885	AI684508 U81800	AI292123	AI458014	AA564822	BG165011	U28386	K02581	AA312511	AI525822	AI733461	AB000277		X02308	M91670	AA719022	AI761506	H06350	AF011468	AW016409		X70940	AI652030	AI861913	AA577678
755	797 715	774	743	775	292	742	713	719	759	772	783		712	209	208	792	793	720	714	·	765	791	703	757
780	781 782	783	784	785	786	787	788	789	280	791	792		793	794	795	796	797	798	799		800	801	802	803

Table 1 (Continued)

(enb	0	Protein	Protein	Protein	Protein	Protein	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Protein	Transcript	Transcript	Protein	Transcript	Transcript	Protein	Transcript	Transcript	Protein	Transcript	Transcript	-	Transcript
DNA segment on chromosome 21 (unique)	chromosome 21 open reading frame 70	nknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	ESTs	hypothetical protein FLJ36779	hypothetical protein FLJ36779	Homo sapiens cDNA FLJ13017 fis,	clone NT2RP3000628	Homo sapiens cDNA FLJ13017 fis, clone NT2RP3000628
Hs.110757	Hs.126522	NOLL	NOLL	NULL	NULL	NULL	NOLL	NOLL	NOLL	NOLL	NULL	NOLL	NOLL	NOLL	Hs.196042	Hs.212613	Hs.212613	Hs.301858		Hs.301858									
q22.3	q22.3	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	q23.2	p21.31	p24.3	q34.3	q34.3	p31.3		p31.3									
21	21	<del>-</del>	<b>~</b>	~	~	<del></del>	<del></del>	<del>-</del>	<del></del>	<del>-</del>	<del>-</del>	~	<b>←</b>	က	က	ග	တ	က	တ	တ	က	တ	တ	က	တ	တ	<del>-</del>		~
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	primary	primary	primary	metastatic	metastatic	metastatic	primary	primary	primary	primary		primary
prostate	prostate	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	breast	colon	colon	colon	colon	colon	colon	lung		gun
AI860822	A1983544	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	R62346	AA663786	AI962335	W25552	W25552	A1962335	W25552	W25552	AI962335	W25552	W25552	AI962335	W25552	W25552	AK022113		AK022113
781	790	120	120	120	120	120	120	120	120	120	120	120	120	197	194	227	227	11	101	101	334	393	393	301	328	328	527		527
804	802	908	807	808	808	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	6	837

																	-	0 27 0 0		0,20,
Protein	Transcript	Transcript		Transcript	Transcript		Protein		Transcript	Transcript	Protein	Protein	Protein .	Protein	Protein	Transcript	Transcript	Protein	Transcript	Transcript
ESTs	ESTs	ESTs, Weakly similar to hypothetical	protein FLJ20837 [Homo sapiens] [H.sapiens]	ESTS	Homo sapiens cDNA FLJ14180 fis,	clone NT2RP2003799	Homo sapiens cDNA FLJ14180 fis,	CIOLIE IN ZAPACIOS/88	unknown	ESTs	hypothetical gene supported by BC007071									
Hs.125249	Hs.125249	Hs.144264		Hs.130107	Hs.296753		Hs.296753		NOLL	Hs.373550	Hs.117305									
p15.1	p15.1	p13.2		q22.3	q21.11		q21.11		q13.3	p11.31	q31.1									
3	2	ည		∞	∞		∞		ω	48	<del></del>	₹.	~	~	~	_	~	<del>-</del>	_	~
primary	primary	primary		primary	primary		primary		primary	primary	metastatic									
lung	i gun	lung		lung	lung		lung		lung	bun	prostate									
AA383208	AA383208	C00851		AA904882	AK024242		AK024242		AF232217	AI146765	N29457									
458	458	519		505	529		529		555	513	753	753	753	753	753	753	753	753	753	753
833	834	835		836	837		838		839	840	841	842	843	844	845	846	847	848	849	820

ipt	<u>io</u>	<u>i</u>	<u>ā</u> .	_	ij	_	_	•	_		Q		_		_		<u>_</u>		_		=		E		=	
Transcript	Transcript	Transcript	Transcript	Protein	<b>Transcript</b>	Protein	Protein		Protein		Protein0		Protein													
hypothetical gene supported by BC007071	unknown	unknown	Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds			
Hs.117305	Hs.117305	Hs.117305	Hs.117305	NOLL	NULL	Hs.72363	Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363	
q31.1	q31.1	q31.1	q31.1	p15.1	p15.1	q32.31	a32.31		q32.31																	
~	~	~	_	IJ	ည	4	14		14		7		14		7		4		4		14		4		4	
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic	
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate	
N29457	N29457	N29457	N29457	AI750154	AI750154	H04885	H04885		H04885		H04885		H04885		H04885		H04885		H04885		H04885		H04885		H04885	
753	753	753	753	705	705	755	755	}	755		755		755		755		755		755		755		755		755	
851	852	853	854	855	856	857	858		829		860		861		862		863		864		865		998		867	

Protein	Protein	Protein	Protein0		LIOCAL	Protein		Protein		Protein		Protein		Protein		Protein		Protein		Protein		Protein		Protein		Protein	
	Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds
Hs.72363	Hs.72363	Hs.72363	Hs.72363	He 77363	13.14500	Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363	
q32.31	q32.31	q32.31	q32.31	430 31	905.0	q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31	
4	4	4	4	14	t	4		4		7		14		4		74		4		7		4		4		4	
metastatic	metastatic	metastatic	metastatic	metactatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic		metastatic	
prostate	prostate	prostate	prostate	nrostata		prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate		prostate	
H04885	H04885	H04885	H04885	H04885		H04885		H04885	1	H04885		H04885		H04885		H04885		H04885		H04885	-	H04885		H04885		H04885	
755	755	755	755	755		755	į	755	1	755	1	755	1	755	!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!	755	1	755	1	755	1 1 1	755		755	! !	755	
898	698	820	871	872	] ;	873	į	874	!	8/2	ļ	876	į	877		878	į	879		880		881		882		883	

Table 1 (Continued)

Protein	Transcript	Protein	Protein	Transcript	Protein	Transcript	Transcript		Transcript	Transcript		Transcript	Transcript		Transcript	Transcrint		Transcript	Transcript
Homo sapiens, clone MGC:16771	Homo sapiens, clone MGC:16771 IMAGE:3907551 mRNA complete cds				IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds		IMAGE:390/331, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds
Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363		Hs.72363	Hs.72363		Hs.72363	Hs.72363		Hs.72363	Hs.72363		Hs.72363	Hs.72363
q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	g32.31	· · · · · · · · · · · · · · · · · · ·	q32.31	q32.31		q32.31	q32.31		q32.31	g32.31	-	q32.31	q32.31
4	4	4	4	4	4	4	4		4	4		4	4		4	4		4	4
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic		metastatic	metastatic		metastatic	metastatic		metastatic	metastatic		metastatic	metastatic
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate		prostate	prostate		prostate	prostate		prostate	prostate		prostate	prostate
H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885		H04885	H04885		H04885	H04885		H04885	H04885		H04885	H04885
755	755	755	755	755	755	755	755	1	755	755	i	755	755	1	755	755		755	755
884	885	988	887	888	889	890	891		892	893		894	895		968	897		898	888

	Transcript	Transcript	Transcript		l ranscript	Transcript		Transcript		Transcript		Transcript	_	Transcript		Transcript	<u>}</u>	<b>Transcript</b>	•	Transcript	-								
	Homo sapiens, clone MGC:16771		IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds		IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds	Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds
	Hs.72363	Hs.72363	Hs.72363	He 77383	13.7 4300	Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363		Hs.72363	
	q32.31	q32.31	q32.31	430 34	905	q32.31		q32.31	0	q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31		q32.31	
	4	4	4	14	_	7		4	;	74		4		4		7		4		4		14		4		4	;	7	
	metastatic	metastatic	metastatic	metastatic		metastatic	•	metastatic		metastatic	•	metastatic		metastatic	;	metastatic		metastatic	•	metastatic	;	metastatic	:	metastatic	;	metastatic		metastatic	
	prostate	prostate	prostate	prostate		prostate	4	prostate	1000	prostate		prostate	•	prostate		prostate	•	prostate		prostate	•	prostate		prostate		prostate	1010	prostate	
	H04885	H04885	H04885	H04885		H04885	1000	H04885	10000	104000	200	H04885		H04885	0.00	H04885		H04885		H04885		H04885	0.00	HU4883	100701	HU4885	20000	104003	
1	755	755	755	755	. [	755	755	00/	755	60	755	( 22	1	CC /	755	00/	, r	00/	755	( 22	756	00/	755	00/	766	CC /	755		
000	006	901	902	903	Č	904	300	202	900	000	000	208	Ċ	808		808	5	2	2,4	- -	ç	2	0,70	2	7,7	0 4	015	2	

Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	Transcript	
Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds Homo sapiens, clone MGC:16771	IMAGE:3907551, mRNA, complete cds						
Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	Hs.72363	
q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	q32.31	
4	4	4	4	4	4	4	4	
metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	metastatic	
prostate	prostate	prostate	prostate	prostate	prostate	prostate	prostate	
H04885	H04885	H04885	H04885	H04885	H04885	H04885	H04885	
755	755	755	755	755	755	755	755	
916	917	918	919	920	921	922	923	

a de la segui de la commencia de la composita de la composito de la composito de la composito de la composito

#### WHAT IS CLAIMED IS:

- 1. A method for diagnosing cancer in a mammal, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.
- 2. The method of claim 1 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

10

20

25

5

- 3. The method of claim 1 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1-805 and 855-923.
- 4. The method of claim 1 wherein said mammal is a human patient.
  - 5. A method for diagnosing cancer or a pre-cancerous condition in a mammal, comprising:
  - (a) obtaining a cell or tissue sample from a mammal suspected of having cancer or a pre-cancerous condition and determining for said sample the gene copy number of a gene of Table 1;
  - (b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

30

6. The method of claim 5 wherein said mammal is a human patient.

7. The method of claim 5 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

- 8. The method of claim 5 wherein the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855–923.
- A method of inhibiting cancer, or a pre-cancerous condition, in a
   mammalian cell, comprising contacting said cell with a molecule that inhibits function of a gene of Table 1.
  - 10. The method of claim 9 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.

15

- 11. The method of claim 9 wherein said molecule inhibits gene function by binding to said gene.
- 20 12. The method of claim 9 wherein said molecule inhibits gene function by binding to an RNA encoded by said gene.
  - 13. The method of claim 9 wherein said molecule inhibits gene function by binding to polypeptide encoded by said gene.
  - 14. The method of claim 9 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.
- 15. The method of claim 9 wherein said cancer is a member selected 30 from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
  - 16. The method of claim 9 wherein said contacting occurs in vivo.

17. A method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

- (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient:
  - (b) administering said test compound to said patient;

5

10

20

25

(c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

- 18. The method of claim 17 wherein said therapeutic activity is anticancer activity.
  - 19. The method of claim 17 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
    - 20. The method of claim 17 wherein said gene product is an RNA.
  - 21. The method of claim 17 wherein said gene product is a polypeptide.
  - 22. The method of claim 21 wherein said determination of said polypeptide is a determination of an enzyme activity.
- 23. The method of claim 17 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.

24. The method of claim 17 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

25. A method for identifying an antineoplastic agent, comprising:

5

15

20

- (a) contacting a test compound with a cell that expresses a gene of Table 1; and
- (b) determining a change in gene expression as a result of said contacting;

whereby said change in said gene expression identifies said test compound as an antineoplastic agent.

- 26. The method of claim 25 wherein said change in expression is a decrease in expression.
  - 27. The method of claim 25 wherein said contacting occurs in vivo.
- 28. The method of claim 25 wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
- 29. The method of claim 25 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, ribozyme, an siRNA, a small organic molecule and an antibody.
- 30. A method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous.
- 31. The method of claim 30 wherein said elevated expression is an elevated copy number of the gene.

32. The method of claim 30 wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

- 33. A method for identifying a compound as an anti-neoplastic agent,comprising:
  - (a) contacting a test compound with a polypeptide encoded by a gene of Table 1,
  - (b) determining a change in a biological activity of said polypeptide due to said contacting,
- wherein a change in activity identifies said test compound as an agent having antineoplastic activity.
  - 34. The method of claim 33 wherein said gene of Table encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.

and the and the same of the party and the same

- 35. The method of claim 33 wherein said change in biological activity is a decrease in biological activity.
- 36. The method of claim 33 wherein said biological activity is an enzyme activity.

15

- 37. The method of claim 36 wherein said enzyme is selected from kinase, protease, peptidase, phosphodiesterase, phosphotase, dehydrogenase, reductase, carboxylase. transferase, deacetylase and polymerase.
  - 38. The method of claim 37 wherein said kinase is a protein kinase.
- 39. The method of claim 37 wherein said kinase is a serine or 30 threonine kinase.

40. The method of claim 37 wherein said kinase is a receptor tyrosine protein kinase.

- 41. The method of claim 37 wherein said protease is a serine protease, cysteine protease or aspartic acid protease.
  - 42. The method of claim 37 wherein said transferase is a methyltransferase.
- 43. The method of claim 42 wherein said methyl transferase is a cytidine methyltransferase or an adenine methyltransferase.

15

- 44. The method of claim 37 wherein said deacetylase is a histone deacetylase.
- 45. The method of claim 37 wherein said carboxylase is a  $\gamma$ -carboxylase.
  - 46. The method of claim 37 wherein said peptidase is a zinc peptidase.
- 47. The method of claim 37 wherein said polymerase is a DNA polymerase.
- 48. The method of claim 37 wherein said polymerase is a RNA 25 polymerase.
  - 49. The method of claim 33 wherein said biological activity is a membrane transport activity.
- 50. The method of claim 33 wherein said polypeptide is a cation channel protein, an anion channel protein, a gated-ion channel protein or an ABC transporter protein.

51. The method of claim 33 wherein said polypeptide is an integrin.

52. The method of claim 33 wherein said polypeptide is a Cytochrome P450 enzyme.

5

- 53. The method of claim 33 wherein said polypeptide is a nuclear hormone receptor.
- 54. The method of claim 33 wherein said biological activity is a receptoractivity.
  - 55. The method of claim 33 wherein said receptor is a G-protein-coupled receptor.
- 15 56. The method of claim 33 wherein said polypeptide is contained in a cell.
  - 57. The method of claim 33 wherein said molecule is a member selected from antisense DNA, an antisense RNA, a ribozyme, an siRNA, a small organic molecule and an antibody.
    - 58. The method of claim 57 wherein said antibody is specific for a polypeptide comprising an amino acid sequence of SEQ ID NO: 806 854.
- 59. A method for identifying an anti-neoplastic agent comprising contacting a cancerous cell with a compound found to have anti-neoplastic activity in the method of claim 59 under conditions promoting the growth of said cell and detecting a change in the activity of said cancerous cell.
- 30 60. The method of claim 59 wherein said change in activity is a decrease in the rate of replication of said cancerous cell.

61. The method of claim 59 wherein said change in activity is the death of said cancerous cell.

62. A method for treating cancer comprising contacting a cancerous cell with an agent first identified as having gene modulating activity using the method of claim 25, 33, or 59 and in an amount effective to cause a reduction in cancerous activity of said cell.

5

- 63. The method of claim 62 wherein said cancerous cell is contacted *in* 10 *vivo*.
  - 64. The method of claim 62 wherein said reduction in cancerous activity is a decrease in the rate of proliferation of said cancerous cell.
- 15 65. The method of claim 62 wherein said reduction in cancerous activity is the death of said cancerous cell.
- 66. The method of claim 62 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
  - 67. A method for treating cancer comprising contacting a cancerous cell with an agent having affinity for an expression product of a gene of Table 1 and in an amount effective to cause a reduction in cancerous activity of said cell.
  - 68. The method of claim 67 wherein said expression product is a polypeptide.
- 30 69. The method of claim 67 wherein said molecule is a member selected from antisense DNA, an antisense RNA, a ribozyme, an siRNA, a small organic molecule and an antibody.

70. The method of claim 69 wherein said antibody is specific for a polypeptide comprising an amino acid sequence selected from SEQ ID NO: 806 – 854.

- 71. A method for monitoring the progress of cancer therapy in a patient comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1.
- 72. The method of claim 71 wherein said gene encodes the same gene 10 product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
  - 73. The method of claim 71 wherein said cancer therapy is chemotherapy.
- 74. The method of claim 71 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.
- 75. A method for determining the likelihood of success of cancer therapy in a patient, comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1 wherein a decrease in said expression prior to completion of said cancer therapy is indicative of a likelihood of success of said cancer therapy.
- 76. The method of claim 75 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 805 and 855 923.
  - 77. The method of claim 75 wherein said cancer therapy is chemotherapy.

78. The method of claim 744 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

- 79. A method for producing test data with respect to the anti-neoplastic activity of a compound comprising:
- (a) identifying a test compound as having anti-neoplastic activity using a method of claim 25;
- (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.
- 80. A method for producing test data with respect to the anti-neoplastic activity of a compound comprising:
- (a) identifying a test compound as having anti-neoplastic activity using a method of claim 33;
  - (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.
  - 81. A method for determining the progress of a treatment for cancer in a patient afflicted therewith, following commencement of a cancer treatment on said patient, comprising:
    - (a) determining in said patient a change in expression of one or more genes of Table 1; and
    - (b) determining a change in expression of said gene compared to expression of said one or more determined genes prior to said cancer treatment;

wherein said change in expression indicates progress of said treatment thereby determining the progress of said treatment.

5

10

20

82. The method of claim 81 wherein said change in expression is a decrease in expression and said decrease indicates success of said treatment.

5 83. The method of claim 81 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

#### THIS PAGE BLANK (USPTO)